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| (57) Abstract  |                             |  |   |
| <p>The invention provides human signal peptide-containing proteins (HSPP) and polynucleotides which identify and encode HSPP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of HSPP.</p> |                             |  |   |

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## HUMAN SIGNAL PEPTIDE-CONTAINING PROTEINS

5

### TECHNICAL FIELD

This invention relates to nucleic acid and amino acid sequences of human signal peptide-containing proteins and to the use of these sequences in the diagnosis, treatment, and prevention of cell proliferative disorders including cancer; inflammation; and cardiovascular, neurological, reproductive, and developmental disorders.

### BACKGROUND OF THE INVENTION

Protein transport is essential for cellular function. Transport of a protein may be mediated by a signal peptide located at the amino terminus of the protein itself. The signal peptide is comprised of about ten to twenty hydrophobic amino acids which target the nascent protein from the ribosome to a particular membrane bound compartment such as the endoplasmic reticulum (ER). Proteins targeted to the ER may either proceed through the secretory pathway or remain in any of the secretory organelles such as the ER. Golgi apparatus, or lysosomes. Proteins that transit through the secretory pathway are either secreted into the extracellular space or retained in the plasma membrane. Secreted proteins are often synthesized as inactive precursors that are activated by post-translational processing events during transit through the secretory pathway. Such events include glycosylation, phosphorylation, proteolysis, and removal of the signal peptide by a signal peptidase. Other events that may occur during protein transport include chaperone-dependent unfolding and folding of the nascent protein and interaction of the protein with a receptor or pore complex. Examples of secreted proteins with amino terminal signal peptides are discussed below and include receptors, extracellular matrix molecules, cytokines, hormones, growth and differentiation factors, neuropeptides, vasomediators, phosphokinases, phosphatases, phospholipases, phosphodiesterases, G and Ras-related proteins, ion channels, transporters/pumps, proteases, and transcription factors. (Reviewed in Alberts, B. et al. (1994) Molecular Biology of The Cell, Garland Publishing, New York, NY, pp. 557-560, 582-592.)

G-protein coupled receptors (GPCRs) comprise a superfamily of integral membrane proteins which transduce extracellular signals. GPCRs include receptors for biogenic amines such as dopamine, epinephrine, histamine, glutamate (metabotropic effect), acetylcholine (muscarinic effect), and serotonin; for lipid mediators of inflammation such as prostaglandins, platelet activating factor, and leukotrienes; for peptide hormones such as calcitonin, C5a anaphylatoxin, follicle stimulating hormone, gonadotropin releasing hormone, neurokinin, oxytocin, and thrombin; and for sensory signal mediators such as retinal photopigments and olfactory stimulatory molecules. The structure of these highly conserved receptors consists of seven hydrophobic transmembrane regions, cysteine disulfide bridges between the second and third extracellular loops, an extracellular N-terminus, and a cytoplasmic C-terminus. The N-terminus interacts with ligands, the disulfide bridges interact with agonists and antagonists, and the large third intracellular loop interacts with G proteins to activate second messengers such as cyclic AMP, phospholipase C, inositol triphosphate, or ion channels. (Reviewed in Watson, S. and Arkininstall, S. (1994) The G-protein Linked Receptor Facts Book, Academic Press, San Diego, CA, pp. 2-6; and Bolander, F.F. (1994) Molecular Endocrinology, Academic Press, San Diego, CA, pp. 162-176.)

Other types of receptors include cell surface antigens identified on leukocytic cells of the immune system. These antigens have been identified using systematic, monoclonal antibody (mAb)-based "shot gun" techniques. These techniques have resulted in the production of hundreds of mAbs directed against unknown cell surface leukocytic antigens. These antigens have been grouped into "clusters of differentiation" based on common immunocytochemical localization patterns in various differentiated and undifferentiated leukocytic cell types. Antigens in a given cluster are presumed to identify a single cell surface protein and are assigned a "CD" number. Some of the genes encoding proteins identified by CD antigens have been isolated and characterized as both transmembrane proteins and cell surface proteins anchored to the plasma membrane via covalent attachment to fatty acid-containing glycolipids such as glycosylphosphatidylinositol (GPI). (Reviewed in Barclay, A. N. et al. (1993) The Leucocyte Antigen Facts Book, Academic Press, San Diego, CA, pp. 144-145; Noel, L. S. et al. (1998) *J. Biol. Chem.* 273:3878-3883.)

Tetraspanins are a superfamily of membrane proteins which facilitate the formation



and stability of cell-surface signaling complexes containing lineage-specific proteins, integrins, and other tetraspanins. They are involved in cell activation, proliferation (including cancer), differentiation, adhesion, and motility. These proteins cross the membrane four times, have conserved intracellular – and C-termini and an extracellular, non-conserved hydrophilic domain. Tetraspanins include, e.g., platelet and endothelial cell membrane proteins, leukocyte surface proteins, tissue specific and tumorous antigens, and the retinitis pigmentosa-associated gene peripherin. (Maecker, H.T. et al. (1997) FASEB J. 11:428-442.)

Matrix proteins (MPs) are transmembrane and extracellular proteins which function in formation, growth, remodeling, and maintenance of tissues and as important mediators and regulators of the inflammatory response. The expression and balance of MPs may be perturbed by biochemical changes that result from congenital, epigenetic, or infectious diseases. In addition, MPs affect leukocyte migration, proliferation, differentiation, and activation in the immune response. MPs are frequently characterized by the presence of one or more domains which may include collagen-like domains, EGF-like domains, immunoglobulin-like domains, and fibronectin-like domains. In addition, some MPs are heavily glycosylated. MPs include extracellular proteins such as fibronectin, collagen, and galectin and cell adhesion receptors such as cell adhesion molecules (CAMs), cadherins, and integrins. (Reviewed in Ayad, S. et al. (1994) The Extracellular Matrix Facts Book, Academic Press, San Diego, CA, pp. 2-16; Ruoslahti, E. (1997) *Kidney Int.* 51:1413-1417; Sjaastad, M.D. and Nelson, W.J. (1997) *BioEssays* 19:47-55.)

Lectins are proteins characterized by their ability to bind carbohydrates on cell membranes by means of discrete, modular carbohydrate recognition domains, CRDs. (Kishore, U. et al. (1997) *Matrix Biol.* 15:583-592.) Certain cytokines and membrane-spanning proteins have CRDs which may enhance interactions with extracellular or intracellular ligands, with proteins in secretory pathways, or with molecules in signal transduction pathways. The lipocalin superfamily constitutes a phylogenetically conserved group of more than forty proteins that function by binding to and transporting a variety of physiologically important ligands. (Tanaka, T. et al. (1997) *J. Biol. Chem.* 272:15789-15795; and van't Hof, W. et al. (1997) *J. Biol. Chem.* 272:1837-1841.) Selectins are a family of calcium ion-dependent lectins expressed on inflamed vascular

endothelium and the surface of some leukocytes. (Rossiter, H. et al. (1997) Mol. Med. Today 3:214-222.)

- Protein kinases regulate many different cell proliferation, differentiation, and signaling processes by adding phosphate groups to proteins. Reversible protein phosphorylation is a key strategy for controlling protein functional activity in eukaryotic cells. The high energy phosphate which drives this activation is generally transferred from adenosine triphosphate molecules (ATP) to a particular protein by protein kinases and removed from that protein by protein phosphatases. Phosphorylation occurs in response to extracellular signals, cell cycle checkpoints, and environmental or nutritional stresses.
- 10 Protein kinases may be roughly divided into two groups; protein tyrosine kinases (PTKs) which phosphorylate tyrosine residues, and serine/threonine kinases (STKs) which phosphorylate serine or threonine residues. A few protein kinases have dual specificity. A majority of kinases contain a similar 250-300 amino acid catalytic domain. (Hardie, G. and Hanks, S. (1995) The Protein Kinase Facts Book, Vol I, pp. 7-47, Academic Press,
- 15 San Diego, CA.)

- Protein phosphatases remove phosphate groups from molecules previously modified by protein kinases thus participating in cell signaling, proliferation, differentiation, contacts, and oncogenesis. Protein phosphorylation is a key strategy used to control protein functional activity in eukaryotic cells. The high energy phosphate is
- 20 transferred from ATP to a protein by protein kinases and removed by protein phosphatases. There appear to be three, evolutionarily-distinct protein phosphatase gene families: protein phosphatases (PPs); protein tyrosine phosphatases (PTPs); and acid/alkaline phosphatases (APs). PPs dephosphorylate phosphoserine/threonine residues and are an important regulator of many cAMP mediated, hormone responses in cells.
- 25 PTPs reverse the effects of protein tyrosine kinases and therefore play a significant role in cell cycle and cell signaling processes. Although APs dephosphorylate substrates in vitro, their role in vivo is not well known. (Charbonneau, H. and Tonks, N.K. (1992) Annu. Rev. Cell Biol. 8:463-493.)

- Cyclic nucleotides (cAMP and cGMP) function as intracellular second messengers
- 30 to transduce a variety of extracellular signals, including hormones, light and neurotransmitters. Cyclic nucleotide phosphodiesterases (PDEs) degrade cyclic nucleotides to their corresponding monophosphates, thereby regulating the intracellular

concentrations of cyclic nucleotides and their effects on signal transduction. At least seven families of mammalian PDEs have been identified based on substrate specificity and affinity, sensitivity to cofactors and sensitivity to inhibitory drugs. (Beavo, J.A. (1995) *Physiological Reviews* 75: 725-748.)

5        Phospholipases (PLs) are enzymes that catalyze the removal of fatty acid residues from phosphoglycerides. PLs play an important role in transmembrane signal transduction and are named according to the specific ester bond in phosphoglycerides that is hydrolyzed, i.e., A<sub>1</sub>, A<sub>2</sub>, C or D. PLA<sub>2</sub> cleaves the ester bond at position 2 of the glycerol moiety of membrane phospholipids giving rise to arachidonic acid. Arachidonic acid is  
10 the common precursor to four major classes of eicosanoids, namely prostaglandins, prostacyclins, thromboxanes and leukotrienes. Eicosanoids are signaling molecules involved in the contraction of smooth muscle, platelet aggregation, and pain and inflammatory responses. (Alberts, B. et al. (1994) Molecular Biology of The Cell, Garland Publishing, Inc., New York, NY, pp. 85, 211, 239-240, 642-645.)

15        The nucleotide cyclases, i.e., adenylate and guanylate cyclase, catalyze the synthesis of the cyclic nucleotides, cAMP and cGMP, from ATP and GTP, respectively. They act in concert with phosphodiesterases, which degrade cAMP and cGMP, to regulate the cellular levels of these molecules and their functions. cAMP and cGMP function as intracellular second messengers to transduce a variety of extracellular signals, e.g.,  
20 hormones, and light and neurotransmitters. (Stryer, L. (1988) Biochemistry W.H. Freeman and Co., New York, pp. 975-980, 1029-1035.)

Cytokines are produced in response to cell perturbation. Some cytokines are produced as precursor forms, and some form multimers in order to become active. They are produced in groups and in patterns characteristic of the particular stimulus or disease,  
25 and the members of the group interact with one another and other molecules to produce an overall biological response. Interleukins, neurotrophins, growth factors, interferons, and chemokines are all families of cytokines which work in conjunction with cellular receptors to regulate cell proliferation and differentiation and to affect such activities as leukocyte migration and function, hematopoietic cell proliferation, temperature regulation, acute  
30 response to infections, tissue remodeling, apoptosis, and cell survival. Studies using antibodies or other drugs that modify the activity of a particular cytokine are used to elucidate the roles of individual cytokines in pathology and physiology.

Chemokines, in particular, are small chemoattractant cytokines involved in inflammation, leukocyte proliferation and migration, angiogenesis and angiostasis, regulation of hematopoiesis, HIV infectivity, and stimulation of cytokine secretion. Chemokines generally contain 70-100 amino acids and are subdivided into four

5 subfamilies based on the presence of conserved cysteine-based motifs. (Callard, R. and Gearing, A. (1994) The Cytokine Facts Book, Academic Press, New York, NY, pp. 181-190, 210-213, 223-227.)

Growth and differentiation factors are secreted proteins which function in intercellular communication. Some factors require oligomerization or association with

10 MPs for activity. Complex interactions among these factors and their receptors trigger intracellular signal transduction pathways that stimulate or inhibit cell division, cell differentiation, cell signaling, and cell motility. Most growth and differentiation factors act on cells in their local environment (paracrine signaling). There are three broad classes of growth and differentiation factors. The first class includes the large polypeptide growth

15 factors such as epidermal growth factor, fibroblast growth factor, transforming growth factor, insulin-like growth factor, and platelet-derived growth factor. The second class includes the hematopoietic growth factors such as the colony stimulating factors (CSFs). Hematopoietic growth factors stimulate the proliferation and differentiation of blood cells such as B-lymphocytes, T-lymphocytes, erythrocytes, platelets, eosinophils, basophils,

20 neutrophils, macrophages, and their stem cell precursors. The third class includes small peptide factors such as bombesin, vasopressin, oxytocin, endothelin, transferrin, angiotensin II, vasoactive intestinal peptide, and bradykinin which function as hormones to regulate cellular functions other than proliferation.

Growth and differentiation factors play critical roles in neoplastic transformation of

25 cells in vitro and in tumor progression in vivo. Inappropriate expression of growth factors by tumor cells may contribute to vascularization and metastasis of melanotic tumors. During hematopoiesis, growth factor misregulation can result in anemias, leukemias, and lymphomas. Certain growth factors such as interferon are cytotoxic to tumor cells both in vivo and in vitro. Moreover, some growth factors and growth factor receptors are related

30 both structurally and functionally to oncoproteins. In addition, growth factors affect transcriptional regulation of both proto-oncogenes and oncosuppressor genes. (Reviewed in Pimentel, E. (1994) Handbook of Growth Factors, CRC Press, Ann Arbor, MI, pp. 1-9.)

Proteolytic enzymes or proteases either activate or deactivate proteins by hydrolyzing peptide bonds. Proteases are found in the cytosol, in membrane-bound compartments, and in the extracellular space. The major families are the zinc, serine, cysteine, thiol, and carboxyl proteases.

- 5 Zinc proteases, e.g., carboxypeptidase A, have a zinc ion bound to the active site. These proteases recognize C-terminal residues that contain an aromatic or bulky aliphatic side chain, and hydrolyze the peptide bond adjacent to the C-terminal residues. Serine proteases have an active site serine residue and include digestive enzymes, e.g., trypsin and chymotrypsin, components of the complement and blood-clotting cascades, and
- 10 enzymes that control the degradation and turnover of extracellular matrix (ECM) molecules. Cysteine proteases (e.g. cathepsin) are produced by monocytes, macrophages and other immune cells, and are involved in diverse cellular processes ranging from the processing of precursor proteins to intracellular degradation. Overproduction of these enzymes can cause the tissue destruction associated with rheumatoid arthritis and asthma.
- 15 Thiol proteases, e.g., papain, contain an active site cysteine and are widely distributed within tissues. Carboxyl proteases, e.g., pepsin, are active only under acidic conditions (pH 2 to 3).

- Guanosine triphosphate-binding proteins (G proteins) can be grouped into two major classes: heterotrimeric G proteins and small G proteins. Heterotrimeric G proteins
- 20 interact with GPCRs that respond to hormones, growth factors, neuromodulators, or other signaling molecules. The interaction between GPCR and G protein allows the G protein to exchange GTP for guanosine diphosphate (GDP). This exchange activates the G protein, allowing it to dissociate from the receptor and interact with the its cognate second messenger-generating protein, e.g., adenylate cyclase, guanylate cyclase, phospholipase C,
- 25 or ion channels. The hydrolysis of GTP to GDP by the G protein acts as an on-off switch, terminating the action of the G protein and preparing it to interact with another receptor molecule, thus beginning another round of signal transduction.

- The small G proteins consist of single 21-30 kDa polypeptides. They can be classified into five subfamilies: Ras, Rho, Ran, Rab, and ADP-ribosylation factor. These
- 30 proteins regulate cell growth, cell cycle control, protein secretion, and intracellular vesicle interaction. In particular, the Ras proteins are essential in transducing signals from receptor tyrosine kinases to serine/threonine kinases which control cell growth and

differentiation. Mutant Ras proteins, which bind but can not hydrolyze GTP, are permanently activated and cause continuous cell proliferation or cancer. All five subfamilies share common structural features and four conserved motifs. Most of the membrane-bound G proteins require a carboxy terminal isoprenyl group (CAAX), added posttranslationally, for membrane association and biological activity. The G proteins also have a variable effector region, located between motifs I and II, which is characterized as the interaction site for guanine nucleotide exchange factors or GTPase-activating proteins.

Eukaryotic cells are bound by a membrane and subdivided into membrane-bound compartments. Membranes are impermeable to many ions and polar molecules, therefore transport of these molecules is mediated by ion channels, ion pumps, transport proteins, or pumps. Symporters and antiporters regulate cytosolic pH by transporting ions and small molecules, e.g., amino acids, glucose, and drugs, across membranes; symporters transport small molecules and ions in the same direction, and antiporters, in the opposite direction. Transporter superfamilies include facilitative transporters and active ATP binding cassette transporters involved in multiple-drug resistance and the targeting of antigenic peptides to MHC Class I molecules. These transporters bind to a specific ion or other molecule and undergo conformational changes in order to transfer the ion or molecule across a membrane. Transport can occur by a passive, concentration-dependent mechanism or can be linked to an energy source such as ATP hydrolysis or an ion gradient.

Ion channels, ion pumps, and transport proteins mediate the transport of molecules across cellular membranes. Symporters and antiporters regulate cytosolic pH by transporting ions and small molecules such as amino acids, glucose, and drugs. Symporters transport small molecules and ions unidirectionally, and antiporters, bidirectionally. Transporter superfamilies include facilitative transporters and active ATP-binding cassette transporters which are involved in multiple-drug resistance and the targeting of antigenic peptides to MHC Class I molecules. These transporters bind to a specific ion or other molecule and undergo a conformational change in order to transfer the ion or molecule across the membrane. Transport can occur by a passive, concentration-dependent mechanism or can be linked to an energy source such as ATP hydrolysis. (Reviewed in Alberts, B. et al. (1994) Molecular Biology of The Cell, Garland Publishing, New York, NY, pp. 523-546.)

Ion channels are formed by transmembrane proteins which create a lined passageway across the membrane through which water and ions, such as  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ , and  $\text{Cl}^-$ , enter and exit the cell. For example, chloride channels are involved in the regulation of the membrane electric potential as well as absorption and secretion of ions across the membrane. Chloride channels also regulate the internal pH of membrane-bound organelles.

Ion pumps are ATPases which actively maintain membrane gradients. Ion pumps are classified as P, V, or F according to their structure and function. All have one or more binding sites for ATP in their cytosolic domains. The P-class ion pumps include  $\text{Ca}^{2+}$  ATPase and  $\text{Na}^+/\text{K}^+$  ATPase and function in transporting  $\text{H}^+$ ,  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$  ions. P-class pumps consist of two  $\alpha$  and two  $\beta$  transmembrane subunits. The V- and F-class ion pumps have similar structures and but transport only  $\text{H}^+$ . F class  $\text{H}^+$  pumps mediate transport across the membranes of mitochondria and chloroplasts, while V-class  $\text{H}^+$  pumps regulate acidity inside lysosomes, endosomes, and plant vacuoles.

A family of structurally related intrinsic membrane proteins known as facilitative glucose transporters catalyze the movement of glucose and other selected sugars across the plasma membrane. The proteins in this family contain a highly conserved, large transmembrane domain comprised of 12  $\alpha$ -helices, and several weakly conserved, cytoplasmic and exoplasmic domains (Pessin, J. E., and Bell, G.I. (1992) *Annu. Rev. Physiol.* 54:911-930).

Amino acid transport is mediated by  $\text{Na}^+$  dependent amino acid transporters. These transporters are involved in gastrointestinal and renal uptake of dietary and cellular amino acids and in neuronal reuptake of neurotransmitters. Transport of cationic amino acids is mediated by the system  $y^+$  family and the cationic amino acid transporter (CAT) family. Members of the CAT family share a high degree of sequence homology, and each contains 12-14 putative transmembrane domains (Ito, K. and Groudine, M. (1997) *J. Biol. Chem.* 272:26780-26786).

Proton-coupled, 12 membrane-spanning domain transporters such as PEPT 1 and PEPT 2 are responsible for gastrointestinal absorption and for renal reabsorption of peptides using an electrochemical  $\text{H}^+$  gradient as the driving force. A heterodimeric peptide transporter, consisting of TAP 1 and TAP 2, is associated with antigen processing. Peptide antigens are transported across the membrane of the endoplasmic reticulum so

they can be presented to the major histocompatibility complex class I molecules. Each TAP protein consists of multiple hydrophobic membrane spanning segments and a highly conserved ATP-binding cassette. (Boll, M. et al. (1996) Proc. Natl. Acad. Sci. 93:284-289.)

- 5           Hormones are secreted molecules that travel through the circulation and bind to specific receptors on the surface of, or within, target cells. Although they have diverse biochemical compositions and mechanisms of action, hormones can be grouped into two categories. One category consists of small lipophilic hormones that diffuse through the plasma membrane of target cells, bind to cytosolic or nuclear receptors, and form a
- 10 complex that alters gene expression. Examples of these molecules include retinoic acid, thyroxine, and the cholesterol-derived steroid hormones such as progesterone, estrogen, testosterone, cortisol, and aldosterone. The second category consists of hydrophilic hormones that function by binding to cell surface receptors that transduce signals across the plasma membrane. Examples of such hormones include amino acid derivatives such
- 15 as catecholamines and peptide hormones such as glucagon, insulin, gastrin, secretin, cholecystokinin, adrenocorticotrophic hormone, follicle stimulating hormone, luteinizing hormone, thyroid stimulating hormone, and vasopressin. (See, for example, Lodish et al. (1995) Molecular Cell Biology, Scientific American Books Inc., New York, NY, pp. 856-864.)
- 20           Neuropeptides and vasomediators (NP/VM) comprise a large family of endogenous signaling molecules. Included in this family are neuropeptides and neuropeptide hormones such as bombesin, neuropeptide Y, neurotensin, neuromedin N, melanocortins, opioids, galanin, somatostatin, tachykinins, urotensin II and related peptides involved in smooth muscle stimulation, vasopressin, vasoactive intestinal peptide,
- 25 and circulatory system-borne signaling molecules such as angiotensin, complement, calcitonin, endothelins, formyl-methionyl peptides, glucagon, cholecystokinin and gastrin. NP/VMs can transduce signals directly, modulate the activity or release of other neurotransmitters and hormones, and act as catalytic enzymes in cascades. The effects of NP/VMs range from extremely brief to long-lasting. (Reviewed in Martin, C. R. et al.
- 30 (1985) Endocrine Physiology, Oxford University Press, New York, NY, pp. 57-62.)

Regulatory molecules turn individual genes or groups of genes on and off in response to various inductive mechanisms of the cell or organism; act as transcription factors by determining



whether or not transcription is initiated, enhanced, or repressed; and splice transcripts as dictated in a particular cell or tissue. Although they interact with short stretches of DNA scattered throughout the entire genome, most gene expression is regulated near the site at which transcription starts or within the open reading frame of the gene being expressed. Many of the transcription factors incorporate one of a set of DNA-binding structural motifs, each of which contains either  $\alpha$  helices or  $\beta$  sheets and binds to the major groove of DNA. (Pabo, C.O. and R.T. Sauer (1992) *Ann. Rev. Biochem.* 61:1053-95.) Other domains of transcription factors may form crucial contacts with the DNA. In addition, accessory proteins provide important interactions which may convert a particular protein complex to an activator or a repressor or may prevent binding. (Alberts, B. et al. (1994) Molecular Biology of the Cell, Garland Publishing Co, New York, NY pp. 401-474.)

The discovery of new human signal peptide-containing proteins and the polynucleotides encoding them satisfies a need in the art by providing new compositions which are useful in the diagnosis, prevention, and treatment of cell proliferative disorders including cancer; inflammation; and cardiovascular, neurological, reproductive, and developmental disorders.

### SUMMARY OF THE INVENTION

The invention features substantially purified polypeptides, proteins with signal peptides, referred to collectively as "HSPP" and individually as "HSPP-1", "HSPP-2", "HSPP-3", "HSPP-4", "HSPP-5", "HSPP-6", "HSPP-7", "HSPP-8", "HSPP-9", "HSPP-10", "HSPP-11", "HSPP-12", "HSPP-13", "HSPP-14", "HSPP-15", "HSPP-16", "HSPP-17", "HSPP-18", "HSPP-19", "HSPP-20", "HSPP-21", "HSPP-22", "HSPP-23", "HSPP-24", "HSPP-25", "HSPP-26", "HSPP-27", "HSPP-28", "HSPP-29", "HSPP-30", "HSPP-31", "HSPP-32", "HSPP-33", "HSPP-34", "HSPP-35", "HSPP-36", "HSPP-37", "HSPP-38", "HSPP-39", "HSPP-40", "HSPP-41", "HSPP-42", "HSPP-43", "HSPP-44", "HSPP-45", "HSPP-46", "HSPP-47", "HSPP-48", "HSPP-49", "HSPP-50", "HSPP-51", "HSPP-52", "HSPP-53", "HSPP-54", "HSPP-55", "HSPP-56", "HSPP-57", "HSPP-58", "HSPP-59", "HSPP-60", "HSPP-61", "HSPP-62", "HSPP-63", "HSPP-64", "HSPP-65", "HSPP-66", "HSPP-67", "HSPP-68", "HSPP-69", "HSPP-70", "HSPP-71", "HSPP-72", "HSPP-73", "HSPP-74", "HSPP-75", "HSPP-76", "HSPP-77", "HSPP-78", "HSPP-79", "HSPP-80", "HSPP-81", "HSPP-82", "HSPP-83", "HSPP-84", "HSPP-85", "HSPP-86", "HSPP-87", "HSPP-88", "HSPP-89", "HSPP-90", "HSPP-91", "HSPP-92", "HSPP-93", "HSPP-94", "HSPP-95", "HSPP-96", "HSPP-97", "HSPP-98", "HSPP-99", "HSPP-100", "HSPP-

101", "HSPP-102", "HSPP-103", "HSPP-104", "HSPP-105", "HSPP-106", "HSPP-107",  
"HSPP-108", "HSPP-109", "HSPP-110", "HSPP-111", "HSPP-112", "HSPP-113", "HSPP-  
114", "HSPP-115", "HSPP-116", "HSPP-117", "HSPP-118", "HSPP-119", "HSPP-120",  
"HSPP-121", "HSPP-122", "HSPP-123", "HSPP-124", "HSPP-125", "HSPP-126",  
5 "HSPP-127", "HSPP-128", "HSPP-129", "HSPP-130", "HSPP-131", "HSPP-132",  
"HSPP-133", and "HSPP-134". In one aspect, the invention provides a substantially  
purified polypeptide comprising an amino acid sequence selected from the group  
consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5,  
SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID  
10 NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16,  
SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ  
ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID  
NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID  
NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37,  
15 SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ  
ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID  
NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53,  
SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ  
ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID  
20 NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69,  
SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ  
ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID  
NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85,  
SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ  
25 ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID  
NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID  
NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID  
NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID  
NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID  
30 NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID  
NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID  
NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID

NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134 (SEQ ID NO:1-134), and fragments thereof.

The invention further provides a substantially purified variant having at least 90% amino acid identity to at least one of the amino acid sequences selected from the group consisting of SEQ ID NO:1-134, and fragments thereof. The invention also provides an isolated and purified polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof. The invention also includes an isolated and purified polynucleotide variant having at least 90% polynucleotide sequence identity to the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof.

Additionally, the invention provides an isolated and purified polynucleotide which hybridizes under stringent conditions to the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof. The invention also provides an isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide encoding the polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof.

The invention also provides an isolated and purified polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID

NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268 (SEQ ID NO:135-268), and fragments thereof. The invention further provides an isolated and purified polynucleotide variant having at least 90% polynucleotide sequence identity to the polynucleotide sequence selected from the group consisting of SEQ ID NO:135-268, and fragments thereof. The invention also provides an isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:135-268, and fragments thereof.

The invention also provides a method for detecting a polynucleotide in a sample containing nucleic acids, the method comprising the steps of (a) hybridizing the complement of the polynucleotide sequence to at least one of the polynucleotides of the sample, thereby forming a hybridization complex; and (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of a polynucleotide in the sample. In one aspect, the method further comprises amplifying the polynucleotide prior to hybridization.

The invention further provides an expression vector containing at least a fragment of the polynucleotide encoding the polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof. In another aspect, the expression vector is contained within a host cell.

The invention also provides a method for producing a polypeptide, the method comprising the steps of: (a) culturing the host cell containing an expression vector containing at least a fragment of a polynucleotide under conditions suitable for the expression of the polypeptide; and (b) recovering the polypeptide from the host cell  
5 culture.

The invention also provides a pharmaceutical composition comprising a substantially purified polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof, in conjunction with a suitable pharmaceutical carrier.

10 The invention further includes a purified antibody which binds to a polypeptide selected from the group consisting of SEQ ID NO:1-134, and fragments thereof. The invention also provides a purified agonist and a purified antagonist to the polypeptide.

The invention also provides a method for treating or preventing a disorder associated with decreased expression or activity of HSPP, the method comprising  
15 administering to a subject in need of such treatment an effective amount of a pharmaceutical composition comprising a substantially purified polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof, in conjunction with a suitable pharmaceutical carrier.

The invention also provides a method for treating or preventing a disorder  
20 associated with increased expression or activity of HSPP, the method comprising administering to a subject in need of such treatment an effective amount of an antagonist of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-134, and fragments thereof.

25

#### BRIEF DESCRIPTION OF THE TABLE

Table 1 shows nucleotide and polypeptide sequence identification numbers (SEQ ID NO), clone identification numbers (clone ID), cDNA libraries, and cDNA fragments used to assemble full-length sequences encoding HSPP.

30 Table 2 shows features of each polypeptide sequence, including predicted signal peptide sequences, and methods and algorithms used for identification of HSPP.

Table 3 shows the tissue-specific expression patterns of each nucleic acid sequence as determined by northern analysis, diseases, disorders, or conditions associated with these tissues, and the vector into which each cDNA was cloned.

Table 4 describes the tissues used to construct the cDNA libraries from which  
5 Incyte cDNA clones encoding HSPP were isolated.

Table 5 shows the programs, their descriptions, references, and threshold parameters used to analyze HSPP.

Table 6 shows the regions of the full-length nucleotide sequences of HSPP to which cDNA fragments of Table 1 correspond.

10

### DESCRIPTION OF THE INVENTION

Before the present proteins, nucleotide sequences, and methods are described, it is understood that this invention is not limited to the particular machines, materials and methods described, as these may vary. It is also to be understood that the terminology  
15 used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise.  
20 Thus, for example, a reference to "a host cell" includes a plurality of such host cells, and a reference to "an antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this  
25 invention belongs. Although any machines, materials, and methods similar or equivalent to those described herein can be used to practice or test the present invention, the preferred machines, materials and methods are now described. All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines, protocols, reagents and vectors which are reported in the publications and which might be used in connection with  
30 the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

## DEFINITIONS

“HSPP” refers to the amino acid sequences of substantially purified HSPP obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and preferably the human species, from any source, whether natural,  
5 synthetic, semi-synthetic, or recombinant.

The term “agonist” refers to a molecule which, when bound to HSPP, increases or prolongs the duration of the effect of HSPP. Agonists may include proteins, nucleic acids, carbohydrates, or any other molecules which bind to and modulate the effect of HSPP.

An “allelic variant” is an alternative form of the gene encoding HSPP. Allelic  
10 variants may result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. Any given natural or recombinant gene may have none, one, or many allelic forms. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these  
15 types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

“Altered” nucleic acid sequences encoding HSPP include those sequences with deletions, insertions, or substitutions of different nucleotides, resulting in a polynucleotide the same as HSPP or a polypeptide with at least one functional characteristic of HSPP.  
20 Included within this definition are polymorphisms which may or may not be readily detectable using a particular oligonucleotide probe of the polynucleotide encoding HSPP, and improper or unexpected hybridization to allelic variants, with a locus other than the normal chromosomal locus for the polynucleotide sequence encoding HSPP. The encoded protein may also be “altered,” and may contain deletions, insertions, or substitutions of  
25 amino acid residues which produce a silent change and result in a functionally equivalent HSPP. Deliberate amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the biological or immunological activity of HSPP is retained. For example, negatively charged amino acids may include aspartic acid and glutamic acid,  
30 positively charged amino acids may include lysine and arginine, and amino acids with uncharged polar head groups having similar hydrophilicity values may include leucine,

isoleucine, and valine; glycine and alanine; asparagine and glutamine; serine and threonine; and phenylalanine and tyrosine.

The terms "amino acid" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide, or protein sequence, or a fragment of any of these, and to naturally occurring  
5 or synthetic molecules. In this context, "fragments," "immunogenic fragments," or "antigenic fragments" refer to fragments of HSPP which are preferably at least 5 to about 15 amino acids in length, most preferably at least 14 amino acids, and which retain some biological activity or immunological activity of HSPP. Where "amino acid sequence" is recited to refer to an amino acid sequence of a naturally occurring protein molecule,  
10 "amino acid sequence" and like terms are not meant to limit the amino acid sequence to the complete native amino acid sequence associated with the recited protein molecule.

"Amplification" relates to the production of additional copies of a nucleic acid sequence. Amplification is generally carried out using polymerase chain reaction (PCR) technologies well known in the art.

15 The term "antagonist" refers to a molecule which, when bound to HSPP, decreases the amount or the duration of the effect of the biological or immunological activity of HSPP. Antagonists may include proteins, nucleic acids, carbohydrates, antibodies, or any other molecules which decrease the effect of HSPP.

The term "antibody" refers to intact molecules as well as to fragments thereof, such  
20 as Fab, F(ab')<sub>2</sub>, and Fv fragments, which are capable of binding the epitopic determinant. Antibodies that bind HSPP polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the translation of RNA, or synthesized chemically, and can be  
25 conjugated to a carrier protein if desired. Commonly used carriers that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

The term "antigenic determinant" refers to that fragment of a molecule (i.e., an epitope) that makes contact with a particular antibody. When a protein or a fragment of a  
30 protein is used to immunize a host animal, numerous regions of the protein may induce the production of antibodies which bind specifically to antigenic determinants (given regions or three-dimensional structures on the protein). An antigenic determinant may compete



with the intact antigen (i.e., the immunogen used to elicit the immune response) for binding to an antibody.

The term "antisense" refers to any composition containing a nucleic acid sequence which is complementary to the "sense" strand of a specific nucleic acid sequence.

- 5 Antisense molecules may be produced by any method including synthesis or transcription. Once introduced into a cell, the complementary nucleotides combine with natural sequences produced by the cell to form duplexes and to block either transcription or translation. The designation "negative" can refer to the antisense strand, and the designation "positive" can refer to the sense strand.

- 10 The term "biologically active," refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule. Likewise, "immunologically active" refers to the capability of the natural, recombinant, or synthetic HSPP, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

- 15 The terms "complementary" or "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence "5' A-G-T 3'" bonds to the complementary sequence "3' T-C-A 5'." Complementarity between two single-stranded molecules may be "partial," such that only some of the nucleic acids bind, or it may be "complete," such that total complementarity exists between the single stranded molecules.

- 20 The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands. This is of particular importance in amplification reactions, which depend upon binding between nucleic acids strands, and in the design and use of peptide nucleic acid (PNA) molecules.

- A "composition comprising a given polynucleotide sequence" or a "composition comprising a given amino acid sequence" refer broadly to any composition containing the given polynucleotide or amino acid sequence. The composition may comprise a dry formulation or an aqueous solution. Compositions comprising polynucleotide sequences encoding HSPP or fragments of HSPP may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be associated with a stabilizing agent
- 25 such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).
- 30

“Consensus sequence” refers to a nucleic acid sequence which has been resequenced to resolve uncalled bases, extended using XL-PCR kit (Perkin-Elmer, Norwalk CT) in the 5' and/or the 3' direction, and resequenced, or which has been assembled from the overlapping sequences of more than one Incyte Clone using a  
5 computer program for fragment assembly, such as the GELVIEW Fragment Assembly system (GCG, Madison WI). Some sequences have been both extended and assembled to produce the consensus sequence.

The term “correlates with expression of a polynucleotide” indicates that the detection of the presence of nucleic acids, the same or related to a nucleic acid sequence  
10 encoding HSPP, by northern analysis is indicative of the presence of nucleic acids encoding HSPP in a sample, and thereby correlates with expression of the transcript from the polynucleotide encoding HSPP.

A “deletion” refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

15 The term “derivative” refers to the chemical modification of a polypeptide sequence, or a polynucleotide sequence. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is  
20 one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

The term “similarity” refers to a degree of complementarity. There may be partial similarity or complete similarity. The word “identity” may substitute for the word “similarity.” A partially complementary sequence that at least partially inhibits an  
25 identical sequence from hybridizing to a target nucleic acid is referred to as “substantially similar.” The inhibition of hybridization of the completely complementary sequence to the target sequence may be examined using a hybridization assay (Southern or northern blot, solution hybridization, and the like) under conditions of reduced stringency. A substantially similar sequence or hybridization probe will compete for and inhibit the  
30 binding of a completely similar (identical) sequence to the target sequence under conditions of reduced stringency. This is not to say that conditions of reduced stringency are such that non-specific binding is permitted, as reduced stringency conditions require

that the binding of two sequences to one another be a specific (i.e., a selective) interaction. The absence of non-specific binding may be tested by the use of a second target sequence which lacks even a partial degree of complementarity (e.g., less than about 30% similarity or identity). In the absence of non-specific binding, the substantially similar sequence or  
5 probe will not hybridize to the second non-complementary target sequence.

The phrases "percent identity" or "% identity" refer to the percentage of sequence similarity found in a comparison of two or more amino acid or nucleic acid sequences. Percent identity can be determined electronically, e.g., by using the MEGALIGN program (DNASTAR, Madison WI) which creates alignments between two or more sequences  
10 according to methods selected by the user, e.g., the clustal method. (See, e.g., Higgins, D.G. and P.M. Sharp (1988) *Gene* 73:237-244.) The clustal algorithm groups sequences into clusters by examining the distances between all pairs. The clusters are aligned pairwise and then in groups. The percentage similarity between two amino acid sequences, e.g., sequence A and sequence B, is calculated by dividing the length of  
15 sequence A, minus the number of gap residues in sequence A, minus the number of gap residues in sequence B, into the sum of the residue matches between sequence A and sequence B, times one hundred. Gaps of low or of no similarity between the two amino acid sequences are not included in determining percentage similarity. Percent identity between nucleic acid sequences can also be counted or calculated by other methods known  
20 in the art, e.g., the Jotun Hein method. (See, e.g., Hein, J. (1990) *Methods Enzymol.* 183:626-645.) Identity between sequences can also be determined by other methods known in the art, e.g., by varying hybridization conditions.

"Human artificial chromosomes" (HACs) are linear microchromosomes which may contain DNA sequences of about 6 kb to 10 Mb in size, and which contain all of the  
25 elements required for stable mitotic chromosome segregation and maintenance.

The term "humanized antibody" refers to antibody molecules in which the amino acid sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

"Hybridization" refers to any process by which a strand of nucleic acid binds with  
30 a complementary strand through base pairing.

The term "hybridization complex" refers to a complex formed between two nucleic acid sequences by virtue of the formation of hydrogen bonds between complementary

bases. A hybridization complex may be formed in solution (e.g.,  $C_0t$  or  $R_0t$  analysis) or formed between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized on a solid support (e.g., paper, membranes, filters, chips, pins or glass slides, or any other appropriate substrate to which cells or their nucleic acids have  
5 been fixed).

The words "insertion" or "addition" refer to changes in an amino acid or nucleotide sequence resulting in the addition of one or more amino acid residues or nucleotides, respectively, to the sequence found in the naturally occurring molecule.

"Immune response" can refer to conditions associated with inflammation, trauma,  
10 immune disorders, or infectious or genetic disease, etc. These conditions can be characterized by expression of various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect cellular and systemic defense systems.

The term "microarray" refers to an arrangement of distinct polynucleotides on a substrate.

15 The terms "element" or "array element" in a microarray context, refer to hybridizable polynucleotides arranged on the surface of a substrate.

The term "modulate" refers to a change in the activity of HSPP. For example, modulation may cause an increase or a decrease in protein activity, binding characteristics, or any other biological, functional, or immunological properties of HSPP.

20 The phrases "nucleic acid" or "nucleic acid sequence," as used herein, refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material. In this context, "fragments" refers  
25 to those nucleic acid sequences which, comprise a region of unique polynucleotide sequence that specifically identifies SEQ ID NO:135-268, for example, as distinct from any other sequence in the same genome. For example, a fragment of SEQ ID NO:135-268 is useful in hybridization and amplification technologies and in analogous methods that distinguish SEQ ID NO:135-268 from related polynucleotide sequences. A fragment of  
30 SEQ ID NO:135-268 is at least about 15-20 nucleotides in length. The precise length of the fragment of SEQ ID NO:135-268 and the region of SEQ ID NO:135-268 to which the fragment corresponds are routinely determinable by one of ordinary skill in the art based

on the intended purpose for the fragment. In some cases, a fragment, when translated, would produce polypeptides retaining some functional characteristic, e.g., antigenicity, or structural domain characteristic, e.g., ATP-binding site, of the full-length polypeptide.

The terms "operably associated" or "operably linked" refer to functionally related  
5 nucleic acid sequences. A promoter is operably associated or operably linked with a coding sequence if the promoter controls the translation of the encoded polypeptide. While operably associated or operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements, e.g., repressor genes, are not contiguously linked to the sequence encoding the polypeptide but still bind to operator  
10 sequences that control expression of the polypeptide.

The term "oligonucleotide" refers to a nucleic acid sequence of at least about 6 nucleotides to 60 nucleotides, preferably about 15 to 30 nucleotides, and most preferably about 20 to 25 nucleotides, which can be used in PCR amplification or in a hybridization assay or microarray. "Oligonucleotide" is substantially equivalent to the terms  
15 "amplimer," "primer," "oligomer," and "probe," as these terms are commonly defined in the art.

"Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers  
20 solubility to the composition. PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation, and may be pegylated to extend their lifespan in the cell.

The term "sample" is used in its broadest sense. A sample suspected of containing nucleic acids encoding HSPP, or fragments thereof, or HSPP itself, may comprise a bodily  
25 fluid; an extract from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

The terms "specific binding" or "specifically binding" refer to that interaction between a protein or peptide and an agonist, an antibody, or an antagonist. The interaction  
30 is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the presence of a polypeptide containing the epitope A, or the

presence of free unlabeled A, in a reaction containing free labeled A and the antibody will reduce the amount of labeled A that binds to the antibody.

The term "stringent conditions" refers to conditions which permit hybridization between polynucleotides and the claimed polynucleotides. Stringent conditions can be defined by salt concentration, the concentration of organic solvent, e.g., formamide, temperature, and other conditions well known in the art. In particular, stringency can be increased by reducing the concentration of salt, increasing the concentration of formamide, or raising the hybridization temperature.

The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least about 60% free, preferably about 75% free, and most preferably about 90% free from other components with which they are naturally associated.

A "substitution" refers to the replacement of one or more amino acids or nucleotides by different amino acids or nucleotides, respectively.

"Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters, chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

"Transformation" describes a process by which exogenous DNA enters and changes a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected based on the type of host cell being transformed and may include, but is not limited to, viral infection, electroporation, heat shock, lipofection, and particle bombardment. The term "transformed" cells includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "variant" of HSPP polypeptides refers to an amino acid sequence that is altered by one or more amino acid residues. The variant may have "conservative" changes, wherein a substituted amino acid has similar structural or chemical properties (e.g.,

replacement of leucine with isoleucine). More rarely, a variant may have “nonconservative” changes (e.g., replacement of glycine with tryptophan). Analogous minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which amino acid residues may be substituted, inserted, or deleted without  
 5 abolishing biological or immunological activity may be found using computer programs well known in the art, for example, LASERGENE software (DNASTAR).

The term “variant,” when used in the context of a polynucleotide sequence, may encompass a polynucleotide sequence related to HSPP. This definition may also include, for example, “allelic” (as defined above), “splice,” “species,” or “polymorphic” variants.  
 10 A splice variant may have significant identity to a reference molecule, but will generally have a greater or lesser number of polynucleotides due to alternate splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or an absence of domains. Species variants are polynucleotide sequences that vary from one species to another. The resulting polypeptides generally will  
 15 have significant amino acid identity relative to each other. A polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass “single nucleotide polymorphisms” (SNPs) in which the polynucleotide sequence varies by one base. The presence of SNPs may be indicative of, for example, a certain population, a disease state,  
 20 or a propensity for a disease state.

## THE INVENTION

The invention is based on the discovery of new human signal peptide-containing proteins (HSPP), the polynucleotides encoding HSPP, and the use of these compositions  
 25 for the diagnosis, treatment, or prevention of cell proliferative disorders including cancer; inflammation; and cardiovascular, neurological, reproductive, and developmental disorders.

Table 1 lists the Incyte Clones used to derive full length nucleotide sequences encoding HSPP. Columns 1 and 2 show the sequence identification numbers (SEQ ID  
 30 NO) of the amino acid and nucleic acid sequences, respectively. Column 3 shows the Clone ID of the Incyte Clone in which nucleic acids encoding each HSPP were identified, and column 4, the cDNA libraries from which these clones were isolated. Column 5

shows Incyte clones, their corresponding cDNA libraries, and shotgun sequences. The clones and shotgun sequences are part of the consensus nucleotide sequence of each HSPP and are useful as fragments in hybridization technologies.

Table 6 shows the regions of the full-length nucleotide sequences of HSPP to which cDNA fragments of Table 1 correspond. Column 1 lists nucleotide sequence identifiers and column 2 shows the clone ID of the Incyte clone in which nucleic acids encoding each HSPP were identified. Column 3 shows Incyte clones and shotgun sequences which are part of the consensus nucleotide sequence of each HSPP and are useful as fragments in hybridization technologies. Column 4 lists the starting nucleotide position and column 5 the ending nucleotide position of the region of the full-length HSPP to which the cDNA fragment corresponds.

The columns of Table 2 show various properties of the polypeptides of the invention: column 1 references the SEQ ID NO; column 2 shows the number of amino acid residues in each polypeptide; column 3, potential phosphorylation sites; column 4, potential glycosylation sites; column 5, the amino acid residues comprising signature sequences and motifs; column 6, the identity of each protein; and column 7, analytical methods used to identify each HSPP as a signal peptide-containing protein. Note that in column 5, the first line of each cell lists the amino acid residues comprising predicted signal peptide sequences. Additional identifying motifs or signatures are also listed in column 5. Of particular note is the presence of a glycosyl hydrolase family 9 active site signature in SEQ ID NO:126, a ribosomal protein S18 signature in SEQ ID NO:127, an adrenodoxin family iron-sulfur binding region signature and a cytochrome c family heme-binding site signature in SEQ ID NO:132, and a urotensin II signature sequence in SEQ ID NO:96.

Using BLAST, SEQ ID NO:68 (HSPP-68) has been identified as a TWIK-related acid-sensitive K<sup>+</sup> channel, and SEQ ID NO:92 (HSPP-92) has been identified as a tyrosine-specific protein phosphatase. The tyrosine-specific protein phosphatases signature in SEQ ID NO:92 (HSPP-92) from about V328 through about F340 (including the putative active site cysteine residue at C330) was identified using BLOCKS and PRINTS. Also of note is the identification of SEQ ID NO:66 (HSPP-66) as a steroid binding protein using BLAST.



The columns of Table 3 show the tissue-specificity and diseases, disorders, or conditions associated with nucleotide sequences encoding HSPP. The first column of Table 3 lists the nucleotide sequence identifiers. The second column lists tissue categories which express HSPP as a fraction of total tissue categories expressing HSPP. The third column lists the diseases, disorders, or conditions associated with those tissues expressing HSPP. The fourth column lists the vectors used to subclone the cDNA library. Of particular note is the expression of SEQ ID NO:200, SEQ ID NO:203, and SEQ ID NO:225 in lung tissues; the expression of SEQ ID NO:212, SEQ ID NO:216, and SEQ ID NO:220 in reproductive tissues; the expression of SEQ ID NO:223 in cancerous tissues; the expression of SEQ ID NO:232 in gastrointestinal tissue, specifically the small intestine or colon (fifteen out of sixteen (93.8%) cDNA libraries); and the expression of SEQ ID NO:224 in cancerous and proliferating tissues. Also of particular interest is the tissue-specific expression of SEQ ID NO:252 and SEQ ID NO:257. SEQ ID NO:252 is derived from OVARTUT01, an ovarian tumor cDNA library and is exclusively expressed in reproductive tumor tissue. SEQ ID NO:257 is derived from THP1AZT01, a 5-aza-2'-deoxycytidine treated human promonocyte cDNA library and is exclusively expressed in hematopoietic tissue.

The following fragments of the nucleotide sequences encoding HSPP are useful in hybridization or amplification technologies to identify SEQ ID NO:135-268 and to distinguish between SEQ ID NO:135-268 and related polynucleotide sequences. The useful fragments are the fragment of SEQ ID NO:230 from about nucleotide 75 to about nucleotide 104; the fragment of SEQ ID NO:231 from about nucleotide 210 to about nucleotide 239; the fragment of SEQ ID NO:232 from about nucleotide 157 to about nucleotide 186; the fragment of SEQ ID NO:233 from about nucleotide 268 to about nucleotide 297; the fragment of SEQ ID NO:234 from about nucleotide 160 to about nucleotide 186; the fragment of SEQ ID NO:235 from about nucleotide 201 to about nucleotide 230; the fragment of SEQ ID NO:236 from about nucleotide 165 to about nucleotide 194; the fragment of SEQ ID NO:237 from about nucleotide 366 to about nucleotide 395; the fragment of SEQ ID NO:238 from about nucleotide 714 to about nucleotide 743; the fragment of SEQ ID NO:239 from about nucleotide 1731 to about nucleotide 1760; the fragment of SEQ ID NO:240 from about nucleotide 419 to about nucleotide 448; the fragment of SEQ ID NO:241 from about nucleotide 494 to about

nucleotide 523; the fragment of SEQ ID NO:242 from about nucleotide 100 to about nucleotide 129; the fragment of SEQ ID NO:243 from about nucleotide 104 to about nucleotide 133; the fragment of SEQ ID NO:244 from about nucleotide 136 to about nucleotide 165; the fragment of SEQ ID NO:245 from about nucleotide 140 to about  
5 nucleotide 169; the fragment of SEQ ID NO:246 from about nucleotide 125 to about nucleotide 154; the fragment of SEQ ID NO:247 from about nucleotide 687 to about nucleotide 758; the fragment of SEQ ID NO:248 from about nucleotide 327 to about nucleotide 398; the fragment of SEQ ID NO:249 from about nucleotide 741 to about nucleotide 785; the fragment of SEQ ID NO:250 from about nucleotide 184 to about  
10 nucleotide 255; the fragment of SEQ ID NO:251 from about nucleotide 165 to about nucleotide 242; the fragment of SEQ ID NO:252 from about nucleotide 271 to about nucleotide 342; the fragment of SEQ ID NO:253 from about nucleotide 1081 to about nucleotide 1152; the fragment of SEQ ID NO:254 from about nucleotide 781 to about nucleotide 852; the fragment of SEQ ID NO:255 from about nucleotide 620 to about  
15 nucleotide 691; the fragment of SEQ ID NO:256 from about nucleotide 872 to about nucleotide 916; the fragment of SEQ ID NO:257 from about nucleotide 242 to about nucleotide 313; the fragment of SEQ ID NO:258 from about nucleotide 595 to about nucleotide 648; the fragment of SEQ ID NO:259 from about nucleotide 163 to about nucleotide 216; the fragment of SEQ ID NO:260 from about nucleotide 244 to about  
20 nucleotide 315; the fragment of SEQ ID NO:261 from about nucleotide 75 to about nucleotide 128; the fragment of SEQ ID NO:262 from about nucleotide 650 to about nucleotide 703; the fragment of SEQ ID NO:263 from about nucleotide 143 to about nucleotide 214; the fragment of SEQ ID NO:264 from about nucleotide 434 to about nucleotide 487; the fragment of SEQ ID NO:265 from about nucleotide 218 to about  
25 nucleotide 271; the fragment of SEQ ID NO:266 from about nucleotide 89 to about nucleotide 145; the fragment of SEQ ID NO:267 from about nucleotide 198 to about nucleotide 254; and the fragment of SEQ ID NO:268 from about nucleotide 10 to about nucleotide 54.

The invention also encompasses HSPP variants. A preferred HSPP variant is one  
30 which has at least about 80%, more preferably at least about 90%, and most preferably at least about 95% amino acid sequence identity to the HSPP amino acid sequence, and which contains at least one functional or structural characteristic of HSPP.

The invention also encompasses polynucleotides which encode HSPP. In a particular embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:135-268, which encodes HSPP.

5 The invention also encompasses a variant of a polynucleotide sequence encoding HSPP. In particular, such a variant polynucleotide sequence will have at least about 80%, more preferably at least about 90%, and most preferably at least about 95% polynucleotide sequence identity to the polynucleotide sequence encoding HSPP. A particular aspect of the invention encompasses a variant of a polynucleotide sequence comprising a sequence  
10 selected from the group consisting of SEQ ID NO:135-268 which has at least about 80%, more preferably at least about 90%, and most preferably at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:135-268. Any one of the polynucleotide variants described above can encode an amino acid sequence which contains at least one functional or structural characteristic of  
15 HSPP.

It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding HSPP, some bearing minimal similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible  
20 variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet genetic code as applied to the polynucleotide sequence of naturally occurring HSPP, and all such variations are to be considered as being specifically disclosed.

Although nucleotide sequences which encode HSPP and its variants are preferably  
25 capable of hybridizing to the nucleotide sequence of the naturally occurring HSPP under appropriately selected conditions of stringency, it may be advantageous to produce nucleotide sequences encoding HSPP or its derivatives possessing a substantially different codon usage, e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or  
30 eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding HSPP and its derivatives without altering the encoded amino acid sequences include the

production of RNA transcripts having more desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of DNA sequences which encode HSPP and HSPP derivatives, or fragments thereof, entirely by synthetic chemistry. After  
5 production, the synthetic sequence may be inserted into any of the many available expression vectors and cell systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce mutations into a sequence encoding HSPP or any fragment thereof.

Also encompassed by the invention are polynucleotide sequences that are capable  
10 of hybridizing to the claimed polynucleotide sequences, and, in particular, to those shown in SEQ ID NO:135-268 and fragments thereof under various conditions of stringency. (See, e.g., Wahl, G.M. and S.L. Berger (1987) *Methods Enzymol.* 152:399-407; Kimmel, A.R. (1987) *Methods Enzymol.* 152:507-511.) For example, stringent salt concentration will ordinarily be less than about 750 mM NaCl and 75 mM trisodium citrate, preferably  
15 less than about 500 mM NaCl and 50 mM trisodium citrate, and most preferably less than about 250 mM NaCl and 25 mM trisodium citrate. Low stringency hybridization can be obtained in the absence of organic solvent, e.g., formamide, while high stringency hybridization can be obtained in the presence of at least about 35% formamide, and most preferably at least about 50% formamide. Stringent temperature conditions will ordinarily  
20 include temperatures of at least about 30°C, more preferably of at least about 37°C, and most preferably of at least about 42°C. Varying additional parameters, such as hybridization time, the concentration of detergent, e.g., sodium dodecyl sulfate (SDS), and the inclusion or exclusion of carrier DNA, are well known to those skilled in the art. Various levels of stringency are accomplished by combining these various conditions as  
25 needed. In a preferred embodiment, hybridization will occur at 30°C in 750 mM NaCl, 75 mM trisodium citrate, and 1% SDS. In a more preferred embodiment, hybridization will occur at 37°C in 500 mM NaCl, 50 mM trisodium citrate, 1% SDS, 35% formamide, and 100 µg/ml denatured salmon sperm DNA (ssDNA). In a most preferred embodiment, hybridization will occur at 42°C in 250 mM NaCl, 25 mM trisodium citrate, 1% SDS, 50  
30 % formamide, and 200 µg/ml ssDNA. Useful variations on these conditions will be readily apparent to those skilled in the art.

The washing steps which follow hybridization can also vary in stringency. Wash stringency conditions can be defined by salt concentration and by temperature. As above, wash stringency can be increased by decreasing salt concentration or by increasing temperature. For example, stringent salt concentration for the wash steps will preferably be less than about 30 mM NaCl and 3 mM trisodium citrate, and most preferably less than about 15 mM NaCl and 1.5 mM trisodium citrate. Stringent temperature conditions for the wash steps will ordinarily include temperature of at least about 25°C, more preferably of at least about 42°C, and most preferably of at least about 68°C. In a preferred embodiment, wash steps will occur at 25°C in 30 mM NaCl, 3 mM trisodium citrate, and 0.1% SDS. In a more preferred embodiment, wash steps will occur at 42°C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. In a most preferred embodiment, wash steps will occur at 68°C in 15 mM NaCl, 1.5 mM trisodium citrate, and 0.1% SDS. Additional variations on these conditions will be readily apparent to those skilled in the art.

Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (Perkin-Elmer), thermostable T7 polymerase (Amersham Pharmacia Biotech, Piscataway NJ), or combinations of polymerases and proofreading exonucleases such as those found in the ELONGASE amplification system (Life Technologies, Gaithersburg MD). Preferably, sequence preparation is automated with machines such as the Hamilton MICROLAB 2200 (Hamilton, Reno NV), Peltier Thermal Cycler 200 (PTC200; MJ Research, Watertown MA) and the ABI CATALYST 800 (Perkin-Elmer). Sequencing is then carried out using either ABI 373 or 377 DNA sequencing systems (Perkin-Elmer) or the MEGABACE 1000 DNA sequencing system (Molecular Dynamics, Sunnyvale CA). The resulting sequences are analyzed using a variety of algorithms which are well known in the art. (See, e.g., Ausubel, F.M. (1997) Short Protocols in Molecular Biology, John Wiley & Sons, New York NY, unit 7.7; Meyers, R.A. (1995) Molecular Biology and Biotechnology, Wiley VCH, New York NY, pp. 856-853.)

The nucleic acid sequences encoding HSPP may be extended utilizing a partial nucleotide sequence and employing various PCR-based methods known in the art to detect

upstream sequences, such as promoters and regulatory elements. For example, one method which may be employed, restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic DNA within a cloning vector. (See, e.g., Sarkar, G. (1993) PCR Methods Applic. 2:318-322.) Another method, inverse PCR, uses  
5 primers that extend in divergent directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a known genomic locus and surrounding sequences. (See, e.g., Triglia, T. et al. (1988) Nucleic Acids Res. 16:8186.) A third method, capture PCR, involves PCR amplification of DNA fragments adjacent to known sequences in human and yeast artificial chromosome  
10 DNA. (See, e.g., Lagerstrom, M. et al. (1991) PCR Methods Applic. 1:111-119.) In this method, multiple restriction enzyme digestions and ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences are known in the art. (See, e.g., Parker, J.D. et al. (1991) Nucleic Acids Res. 19:3055-306).  
15 Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic DNA. This procedure avoids the need to screen libraries and is useful in finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences, Plymouth MN) or another appropriate  
20 program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the template at temperatures of about 68°C to 72°C.

When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in  
25 which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.

Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic  
30 separation, four different nucleotide-specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the emitted wavelengths. Output/light intensity may be converted to electrical signal using appropriate software (e.g.,

GENOTYPER and SEQUENCE NAVIGATOR, Perkin-Elmer), and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments which may be present in limited amounts in a particular sample.

5 In another embodiment of the invention, polynucleotide sequences or fragments thereof which encode HSPP may be cloned in recombinant DNA molecules that direct expression of HSPP, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be  
10 produced and used to express HSPP.

The nucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter HSPP-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR  
15 reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

In another embodiment, sequences encoding HSPP may be synthesized, in whole  
20 or in part, using chemical methods well known in the art. (See, e.g., Caruthers, M.H. et al. (1980) Nucl. Acids Res. Symp. Ser. 215-223, and Horn, T. et al. (1980) Nucl. Acids Res. Symp. Ser. 225-232.) Alternatively, HSPP itself or a fragment thereof may be synthesized using chemical methods. For example, peptide synthesis can be performed using various solid-phase techniques. (See, e.g., Roberge, J.Y. et al. (1995) Science 269:202-204.)  
25 Automated synthesis may be achieved using the ABI 431A Peptide Synthesizer (Perkin-Elmer). Additionally, the amino acid sequence of HSPP, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

The peptide may be substantially purified by preparative high performance liquid  
30 chromatography. (See, e.g., Chiez, R.M. and F.Z. Regnier (1990) Methods Enzymol. 182:392-421.) The composition of the synthetic peptides may be confirmed by amino acid

analysis or by sequencing. (See, e.g., Creighton, T. (1984) Proteins, Structures and Molecular Properties, WH Freeman, New York NY.)

In order to express a biologically active HSPP, the nucleotide sequences encoding HSPP or derivatives thereof may be inserted into an appropriate expression vector, i.e., a  
5 vector which contains the necessary elements for transcriptional and translational control of the inserted coding sequence in a suitable host. These elements include regulatory sequences, such as enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotide sequences encoding HSPP. Such elements may vary in their strength and specificity. Specific initiation signals may also be  
10 used to achieve more efficient translation of sequences encoding HSPP. Such signals include the ATG initiation codon and adjacent sequences, e.g. the Kozak sequence. In cases where sequences encoding HSPP and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding  
15 sequence, or a fragment thereof, is inserted, exogenous translational control signals including an in-frame ATG initiation codon should be provided by the vector. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used. (See, e.g., Scharf, D. et al. (1994)  
20 Results Probl. Cell Differ. 20:125-162.)

Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding HSPP and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. (See, e.g., Sambrook,  
25 J. et al. (1989) Molecular Cloning. A Laboratory Manual, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel, F.M. et al. (1995) Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, ch. 9, 13, and 16.)

A variety of expression vector/host systems may be utilized to contain and express sequences encoding HSPP. These include, but are not limited to, microorganisms such as  
30 bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with viral expression vectors (e.g., baculovirus); plant cell systems transformed with viral



expression vectors (e.g., cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems. The invention is not limited by the host cell employed.

In bacterial systems, a number of cloning and expression vectors may be selected depending upon the use intended for polynucleotide sequences encoding HSPP. For example, routine cloning, subcloning, and propagation of polynucleotide sequences encoding HSPP can be achieved using a multifunctional E. coli vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or pSPORT1 plasmid (Life Technologies). Ligation of sequences encoding HSPP into the vector's multiple cloning site disrupts the *lacZ* gene, allowing a colorimetric screening procedure for identification of transformed bacteria containing recombinant molecules. In addition, these vectors may be useful for in vitro transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of nested deletions in the cloned sequence. (See, e.g., Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509.) When large quantities of HSPP are needed, e.g. for the production of antibodies, vectors which direct high level expression of HSPP may be used. For example, vectors containing the strong, inducible T5 or T7 bacteriophage promoter may be used.

Yeast expression systems may be used for production of HSPP. A number of vectors containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH, may be used in the yeast Saccharomyces cerevisiae or Pichia pastoris. In addition, such vectors direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign sequences into the host genome for stable propagation. (See, e.g., Ausubel, 1995, supra; Grant et al. (1987) Methods Enzymol. 153:516-54; and Scorer, C. A. et al. (1994) Bio/Technology 12:181-184.)

Plant systems may also be used for expression of HSPP. Transcription of sequences encoding HSPP may be driven viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J. 6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used. (See, e.g., Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al. (1984) Science 224:838-843; and Winter, J. et al. (1991) Results Probl. Cell Differ. 17:85-105.) These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated

transfection. (See, e.g., The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196.)

In mammalian cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, sequences encoding HSPP  
5 may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses HSPP in host cells. (See, e.g., Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. 81:3655-3659.) In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be  
10 used to increase expression in mammalian host cells. SV40 or EBV-based vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are constructed and delivered via conventional delivery methods  
15 (liposomes, polycationic amino polymers, or vesicles) for therapeutic purposes. (See, e.g., Harrington, J.J. et al. (1997) Nat Genet. 15:345-355.)

For long term production of recombinant proteins in mammalian systems, stable expression of HSPP in cell lines is preferred. For example, sequences encoding HSPP can be transformed into cell lines using expression vectors which may contain viral origins of  
20 replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express the  
25 introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in *tk* or *apr*<sup>-</sup> cells, respectively. (See,  
30 e.g., Wigler, M. et al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823.) Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, *dhfr* confers resistance to methotrexate; *neo* confers resistance to

the aminoglycosides, neomycin and G-418; and *als* or *pat* confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. (See, e.g., Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. 77:3567-3570; Colbere-Garapin, F. et al. (1981) J. Mol. Biol. 150:1-14.) Additional selectable genes have been described, e.g., *trpB* and *hisD*,  
5 which alter cellular requirements for metabolites. (See, e.g., Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. 85:8047-8051.) Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP; Clontech),  $\beta$  glucuronidase and its substrate  $\beta$ -glucuronide, or luciferase and its substrate luciferin may be used. These markers can be used not only to identify transformants, but also to quantify the amount of  
10 transient or stable protein expression attributable to a specific vector system. (See, e.g., Rhodes, C.A. (1995) Methods Mol. Biol. 55:121-131.)

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the sequence encoding HSPP is inserted within a marker gene sequence,  
15 transformed cells containing sequences encoding HSPP can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a sequence encoding HSPP under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

20 In general, host cells that contain the nucleic acid sequence encoding HSPP and that express HSPP may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR amplification, and protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies for the detection and/or  
25 quantification of nucleic acid or protein sequences.

Immunological methods for detecting and measuring the expression of HSPP using either specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). A two-site,  
30 monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on HSPP is preferred, but a competitive binding assay may be employed. These and other assays are well known in the art. (See, e.g., Hampton, R. et al.

(1990) Serological Methods, a Laboratory Manual, APS Press, St Paul MN, Sect. IV; Coligan, J. E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New York NY; and Pound, J.D. (1998) Immunochemical Protocols, Humana Press, Totowa NJ).

5       A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding HSPP include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, the sequences encoding  
10 HSPP, or any fragments thereof, may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Pharmacia  
15 Biotech, Promega (Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be used for ease of detection include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with nucleotide sequences encoding HSPP may be cultured  
20 under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode HSPP may be designed to contain signal sequences which direct secretion of HSPP through a prokaryotic  
25 or eukaryotic cell membrane.

In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing  
30 which cleaves a "prepro" form of the protein may also be used to specify protein targeting, folding, and/or activity. Different host cells which have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK,

HEK293, and WI38), are available from the American Type Culture Collection (ATCC, Manassas, VA) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences encoding HSPP may be ligated to a heterologous sequence resulting in translation of a fusion protein in any of the aforementioned host systems. For example, a chimeric HSPP protein containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of HSPP activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG, *c-myc*, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, *c-myc*, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize these epitope tags. A fusion protein may also be engineered to contain a proteolytic cleavage site located between the HSPP encoding sequence and the heterologous protein sequence, so that HSPP may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch 10). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

In a further embodiment of the invention, synthesis of radiolabeled HSPP may be achieved in vitro using the TNT rabbit reticulocyte lysate or wheat germ extract systems (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, preferably <sup>35</sup>S-methionine.

Fragments of HSPP may be produced not only by recombinant production, but also by direct peptide synthesis using solid-phase techniques. (See, e.g., Creighton, supra, pp. 55-60.) Protein synthesis may be performed by manual techniques or by automation. Automated synthesis may be achieved, for example, using the ABI 431A Peptide

Synthesizer (Perkin-Elmer). Various fragments of HSPP may be synthesized separately and then combined to produce the full length molecule.

## THERAPEUTICS

5           Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of HSPP and signal peptide sequences. In addition, chemical and structural similarity, in the context of sequences and motifs, exists between HSPP-66 and prostatic steriod-binding C3 precursor from rat (GI 206453); between HSPP-68 and TWIK-related acid-sensitive K<sup>+</sup>channel from human (GI 2465542); and between HSPP-92  
10 and tyrosine specific protein phosphatases (PROSITE PDOC00323). In addition, the expression of HSPP is closely associated with proliferative, cancerous, inflamed, cardiovascular, nervous, reproductive, hematopoietic/immune, and developmental tissue. Therefore, HSPP appears to play a role in cell proliferative disorders including cancer; inflammation; and cardiovascular,  
15 neurological, reproductive, and developmental disorders. In the treatment of cell proliferative disorders including cancer; inflammation; and cardiovascular, neurological, reproductive, and developmental disorders associated with increased HSPP expression or activity, it is desirable to decrease the expression or activity of HSPP. In the treatment of the above conditions associated with decreased HSPP expression or activity, it is desirable  
20 to increase the expression or activity of HSPP.

          Therefore, in one embodiment, HSPP or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HSPP. Examples of such disorders include, but are not limited to, cell proliferative disorders such as actinic keratosis, arteriosclerosis, atherosclerosis,  
25 bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia,  
30 gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; inflammatory disorders, such as acquired immunodeficiency syndrome (AIDS), Addison's

- disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis,
- 5 dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis,
- 10 polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; cardiovascular disorders including
- 15 disorders of the blood vessels such as arteriovenous fistula, atherosclerosis, hypertension, vasculitis, Raynaud's disease, aneurysms, arterial dissections, varicose veins, thrombophlebitis and phlebothrombosis, and vascular tumors; disorders of the heart such as congestive heart failure, ischemic heart disease, angina pectoris, myocardial infarction, hypertensive heart disease, degenerative valvular heart disease, calcific aortic valve
- 20 stenosis, congenitally bicuspid aortic valve, mitral annular calcification, mitral valve prolapse, rheumatic fever and rheumatic heart disease, infective endocarditis, nonbacterial thrombotic endocarditis, endocarditis of systemic lupus erythematosus, carcinoid heart disease, cardiomyopathy, myocarditis, pericarditis, neoplastic heart disease, and congenital heart disease; and disorders of the lungs such as congenital lung anomalies, atelectasis,
- 25 pulmonary congestion and edema, pulmonary embolism, pulmonary hemorrhage, pulmonary infarction, pulmonary hypertension, vascular sclerosis, obstructive pulmonary disease, restrictive pulmonary disease, chronic obstructive pulmonary disease, emphysema, chronic bronchitis, bronchial asthma, bronchiectasis, bacterial pneumonia, viral and mycoplasmal pneumonia, lung abscess, pulmonary tuberculosis, diffuse
- 30 interstitial diseases, pneumoconioses, sarcoidosis, idiopathic pulmonary fibrosis, desquamative interstitial pneumonitis, hypersensitivity pneumonitis, pulmonary eosinophilia bronchiolitis obliterans-organizing pneumonia, diffuse pulmonary

- hemorrhage syndromes, Goodpasture's syndromes, idiopathic pulmonary hemosiderosis, pulmonary involvement in collagen-vascular disorders, pulmonary alveolar proteinosis, lung tumors, inflammatory and noninflammatory pleural effusions, pneumothorax, and pleural tumors; neurological disorders such as epilepsy, ischemic cerebrovascular disease,
- 5 stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess,
- 10 suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease; prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome; fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other
- 15 developmental disorders of the central nervous system, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis; inherited, metabolic, endocrine, and toxic myopathies; myasthenia gravis, periodic paralysis; mental disorders including mood,
- 20 anxiety, and schizophrenic disorders; akathisia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, and Tourette's disorder; reproductive disorders such as disorders of prolactin production; infertility, including tubal disease, ovulatory defects, and endometriosis; disruptions of the estrous cycle, disruptions of the menstrual cycle, polycystic ovary syndrome, ovarian
- 25 hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancies, and teratogenesis; cancer of the breast, fibrocystic breast disease, and galactorrhea; disruptions of spermatogenesis, abnormal sperm physiology, cancer of the testis, cancer of the prostate, benign prostatic hyperplasia, prostatitis, Peyronie's disease, carcinoma of the male breast, and gynecomastia; and developmental
- 30 disorders, such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy, gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and mental



retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratodermas, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Sydenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract, and sensorineural hearing loss.

In another embodiment, a vector capable of expressing HSPP or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HSPP including, but not limited to, those described above.

In a further embodiment, a pharmaceutical composition comprising a substantially purified HSPP in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HSPP including, but not limited to, those provided above.

In still another embodiment, an agonist which modulates the activity of HSPP may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of HSPP including, but not limited to, those listed above.

In a further embodiment, an antagonist of HSPP may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of HSPP. Examples of such disorders include, but are not limited to, those described above. In one aspect, an antibody which specifically binds HSPP may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissue which express HSPP.

In an additional embodiment, a vector expressing the complement of the polynucleotide encoding HSPP may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of HSPP including, but not limited to, those described above.

In other embodiments, any of the proteins, antagonists, antibodies, agonists, complementary sequences, or vectors of the invention may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act

synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic efficacy with lower dosages of each agent, thus reducing the potential for adverse side effects.

An antagonist of HSPP may be produced using methods which are generally known in the art. In particular, purified HSPP may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind HSPP. Antibodies to HSPP may also be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments, and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are especially preferred for therapeutic use.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, humans, and others may be immunized by injection with HSPP or with any fragment or oligopeptide thereof which has immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include, but are not limited to, Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially preferable.

It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to HSPP have an amino acid sequence consisting of at least about 5 amino acids, and, more preferably, of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein and contain the entire amino acid sequence of a small, naturally occurring molecule. Short stretches of HSPP amino acids may be fused with those of another protein, such as KLH, and antibodies to the chimeric molecule may be produced.

Monoclonal antibodies to HSPP may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique. (See, e.g., Kohler, G. et al. (1975) Nature 256:495-497; Kozbor, D. et al. (1985) J. Immunol. Methods 81:31-42;

Cote, R.J. et al. (1983) Proc. Natl. Acad. Sci. 80:2026-2030; and Cole, S.P. et al. (1984) Mol. Cell Biol. 62:109-120.)

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) Proc. Natl. Acad. Sci. 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; and Takeda, S. et al. (1985) Nature 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce HSPP-specific single chain antibodies. Antibodies with related specificity, but of distinct idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g., Burton D.R. (1991) Proc. Natl. Acad. Sci. 88:10134-10137.)

Antibodies may also be produced by inducing *in vivo* production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature. (See, e.g., Orlandi, R. et al. (1989) Proc. Natl. Acad. Sci. 86: 3833-3837; Winter, G. et al. (1991) Nature 349:293-299.)

Antibody fragments which contain specific binding sites for HSPP may also be generated. For example, such fragments include, but are not limited to, F(ab')<sub>2</sub> fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the F(ab')<sub>2</sub> fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity. (See, e.g., Huse, W.D. et al. (1989) Science 246:1275-1281.)

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between HSPP and its specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering HSPP epitopes is preferred, but a competitive binding assay may also be employed (Pound, *supra*).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for HSPP. Affinity is expressed as an association constant,  $K_a$ , which is defined as the molar concentration of HSPP-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The  $K_a$  determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple HSPP epitopes, represents the average affinity, or avidity, of the antibodies for HSPP. The  $K_a$  determined for a preparation of monoclonal antibodies, which are monospecific for a particular HSPP epitope, represents a true measure of affinity. High-affinity antibody preparations with  $K_a$  ranging from about  $10^9$  to  $10^{12}$  L/mole are preferred for use in immunoassays in which the HSPP-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with  $K_a$  ranging from about  $10^6$  to  $10^7$  L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of HSPP, preferably in active form, from the antibody (Catty, D. (1988) Antibodies, Volume I: A Practical Approach, IRL Press, Washington, DC; Liddell, J. E. and Cryer, A. (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is preferred for use in procedures requiring precipitation of HSPP-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al. supra.)

In another embodiment of the invention, the polynucleotides encoding HSPP, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, the complement of the polynucleotide encoding HSPP may be used in situations in which it would be desirable to block the transcription of the mRNA. In particular, cells may be transformed with sequences complementary to polynucleotides encoding HSPP. Thus, complementary molecules or fragments may be used to modulate HSPP activity, or to achieve regulation of gene function. Such technology is now well known in the art, and

sense or antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding HSPP.

Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids, may be used for delivery of nucleotide  
5 sequences to the targeted organ, tissue, or cell population. Methods which are well known to those skilled in the art can be used to construct vectors to express nucleic acid sequences complementary to the polynucleotides encoding HSPP. (See, e.g., Sambrook, supra; Ausubel, 1995, supra.)

Genes encoding HSPP can be turned off by transforming a cell or tissue with  
10 expression vectors which express high levels of a polynucleotide, or fragment thereof, encoding HSPP. Such constructs may be used to introduce untranslatable sense or antisense sequences into a cell. Even in the absence of integration into the DNA, such vectors may continue to transcribe RNA molecules until they are disabled by endogenous nucleases. Transient expression may last for a month or more with a non-replicating  
15 vector, and may last even longer if appropriate replication elements are part of the vector system.

As mentioned above, modifications of gene expression can be obtained by designing complementary sequences or antisense molecules (DNA, RNA, or PNA) to the control, 5', or regulatory regions of the gene encoding HSPP. Oligonucleotides derived  
20 from the transcription initiation site, e.g., between about positions -10 and +10 from the start site, are preferred. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex  
25 DNA have been described in the literature. (See, e.g., Gee, J.E. et al. (1994) in Huber, B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177.) A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

30 Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target RNA, followed by

endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze endonucleolytic cleavage of sequences encoding HSPP.

Specific ribozyme cleavage sites within any potential RNA target are initially  
5 identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides, corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be  
10 evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

Complementary ribonucleic acid molecules and ribozymes of the invention may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase  
15 phosphoramidite chemical synthesis. Alternatively, RNA molecules may be generated by in vitro and in vivo transcription of DNA sequences encoding HSPP. Such DNA sequences may be incorporated into a wide variety of vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell  
20 lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is  
25 inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

Many methods for introducing vectors into cells or tissues are available and  
30 equally suitable for use in vivo, in vitro, and ex vivo. For ex vivo therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or

by polycationic amino polymers may be achieved using methods which are well known in the art. (See, e.g., Goldman, C.K. et al. (1997) Nature Biotechnology 15:462-466.)

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as dogs, cats, cows, horses, rabbits, monkeys, and most preferably, humans.

An additional embodiment of the invention relates to the administration of a pharmaceutical or sterile composition, in conjunction with a pharmaceutically acceptable carrier, for any of the therapeutic effects discussed above. Such pharmaceutical compositions may consist of HSPP, antibodies to HSPP, and mimetics, agonists, antagonists, or inhibitors of HSPP. The compositions may be administered alone or in combination with at least one other agent, such as a stabilizing compound, which may be administered in any sterile, biocompatible pharmaceutical carrier including, but not limited to, saline, buffered saline, dextrose, and water. The compositions may be administered to a patient alone, or in combination with other agents, drugs, or hormones.

The pharmaceutical compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable pharmaceutically-acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. Further details on techniques for formulation and administration may be found in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing, Easton PA).

Pharmaceutical compositions for oral administration can be formulated using pharmaceutically acceptable carriers well known in the art in dosages suitable for oral administration. Such carriers enable the pharmaceutical compositions to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions, and the like, for ingestion by the patient.

Pharmaceutical preparations for oral use can be obtained through combining active compounds with solid excipient and processing the resultant mixture of granules (optionally, after grinding) to obtain tablets or dragee cores. Suitable auxiliaries can be

added, if desired. Suitable excipients include carbohydrate or protein fillers, such as sugars, including lactose, sucrose, mannitol, and sorbitol; starch from corn, wheat, rice, potato, or other plants; cellulose, such as methyl cellulose, hydroxypropylmethyl-cellulose, or sodium carboxymethylcellulose; gums, including  
5 arabic and tragacanth; and proteins, such as gelatin and collagen. If desired, disintegrating or solubilizing agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, and alginic acid or a salt thereof, such as sodium alginate.

Dragee cores may be used in conjunction with suitable coatings, such as concentrated sugar solutions, which may also contain gum arabic, talc,  
10 polyvinylpyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for product identification or to characterize the quantity of active compound, i.e., dosage.

Pharmaceutical preparations which can be used orally include push-fit capsules  
15 made of gelatin, as well as soft, sealed capsules made of gelatin and a coating, such as glycerol or sorbitol. Push-fit capsules can contain active ingredients mixed with fillers or binders, such as lactose or starches, lubricants, such as talc or magnesium stearate, and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid, or liquid polyethylene glycol with  
20 or without stabilizers.

Pharmaceutical formulations suitable for parenteral administration may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiologically buffered saline. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such  
25 as sodium carboxymethyl cellulose, sorbitol, or dextran. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils, such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate, triglycerides, or liposomes. Non-lipid polycationic amino polymers may also be used for delivery. Optionally, the suspension may also contain  
30 suitable stabilizers or agents to increase the solubility of the compounds and allow for the preparation of highly concentrated solutions.



For topical or nasal administration, penetrants appropriate to the particular barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

The pharmaceutical compositions of the present invention may be manufactured in  
5 a manner that is known in the art, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes.

The pharmaceutical composition may be provided as a salt and can be formed with many acids, including but not limited to, hydrochloric, sulfuric, acetic, lactic, tartaric,  
10 malic, and succinic acid. Salts tend to be more soluble in aqueous or other protonic solvents than are the corresponding free base forms. In other cases, the preferred preparation may be a lyophilized powder which may contain any or all of the following: 1 mM to 50 mM histidine, 0.1% to 2% sucrose, and 2% to 7% mannitol, at a pH range of 4.5 to 5.5, that is combined with buffer prior to use.

15 After pharmaceutical compositions have been prepared, they can be placed in an appropriate container and labeled for treatment of an indicated condition. For administration of HSPP, such labeling would include amount, frequency, and method of administration.

Pharmaceutical compositions suitable for use in the invention include compositions  
20 wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the art.

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells or in animal models such as mice, rats,  
25 rabbits, dogs, or pigs. An animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example HSPP or fragments thereof, antibodies of HSPP, and agonists, antagonists or  
30 inhibitors of HSPP, which ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the ED<sub>50</sub> (the dose therapeutically

effective in 50% of the population) or  $LD_{50}$  (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, and it can be expressed as the  $LD_{50}/ED_{50}$  ratio. Pharmaceutical compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the  $ED_{50}$  with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy. Long-acting pharmaceutical compositions may be administered every 3 to 4 days, every week, or biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about  $0.1 \mu\text{g}$  to  $100,000 \mu\text{g}$ , up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

## 25 **DIAGNOSTICS**

In another embodiment, antibodies which specifically bind HSPP may be used for the diagnosis of disorders characterized by expression of HSPP, or in assays to monitor patients being treated with HSPP or agonists, antagonists, or inhibitors of HSPP. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics. Diagnostic assays for HSPP include methods which utilize the antibody and a label to detect HSPP in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be labeled

by covalent or non-covalent attachment of a reporter molecule. A wide variety of reporter molecules, several of which are described above, are known in the art and may be used.

A variety of protocols for measuring HSPP, including ELISAs, RIAs, and FACS, are known in the art and provide a basis for diagnosing altered or abnormal levels of HSPP expression. Normal or standard values for HSPP expression are established by combining  
5 body fluids or cell extracts taken from normal mammalian subjects, preferably human, with antibody to HSPP under conditions suitable for complex formation. The amount of standard complex formation may be quantitated by various methods, preferably by photometric means. Quantities of HSPP expressed in subject, control, and disease samples  
10 from biopsied tissues are compared with the standard values. Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, the polynucleotides encoding HSPP may be used for diagnostic purposes. The polynucleotides which may be used include oligonucleotide sequences, complementary RNA and DNA molecules, and PNAs. The  
15 polynucleotides may be used to detect and quantitate gene expression in biopsied tissues in which expression of HSPP may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of HSPP, and to monitor regulation of HSPP levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting  
20 polynucleotide sequences, including genomic sequences, encoding HSPP or closely related molecules may be used to identify nucleic acid sequences which encode HSPP. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a conserved motif, and the stringency of the hybridization or amplification (maximal, high, intermediate, or low), will  
25 determine whether the probe identifies only naturally occurring sequences encoding HSPP, allelic variants, or related sequences.

Probes may also be used for the detection of related sequences, and should preferably have at least 50% sequence identity to any of the HSPP encoding sequences. The hybridization probes of the subject invention may be DNA or RNA and may be  
30 derived from the sequence of SEQ ID NO:135-268 or from genomic sequences including promoters, enhancers, and introns of the HSPP gene.

Means for producing specific hybridization probes for DNAs encoding HSPP include the cloning of polynucleotide sequences encoding HSPP or HSPP derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, by radionuclides such as  $^{32}\text{P}$  or  $^{35}\text{S}$ , or by enzymatic labels, such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotide sequences encoding HSPP may be used for the diagnosis of disorders associated with expression of HSPP. Examples of such disorders include, but are not limited to, cell proliferative disorders such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; inflammatory disorders, such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic,

protozoal, and helminthic infections, and trauma; cardiovascular disorders including disorders of the blood vessels such as arteriovenous fistula, atherosclerosis, hypertension, vasculitis, Raynaud's disease, aneurysms, arterial dissections, varicose veins, thrombophlebitis and phlebothrombosis, and vascular tumors; disorders of the heart such as congestive heart failure, ischemic heart disease, angina pectoris, myocardial infarction, hypertensive heart disease, degenerative valvular heart disease, calcific aortic valve stenosis, congenitally bicuspid aortic valve, mitral annular calcification, mitral valve prolapse, rheumatic fever and rheumatic heart disease, infective endocarditis, nonbacterial thrombotic endocarditis, endocarditis of systemic lupus erythematosus, carcinoid heart disease, cardiomyopathy, myocarditis, pericarditis, neoplastic heart disease, and congenital heart disease; and disorders of the lungs such as congenital lung anomalies, atelectasis, pulmonary congestion and edema, pulmonary embolism, pulmonary hemorrhage, pulmonary infarction, pulmonary hypertension, vascular sclerosis, obstructive pulmonary disease, restrictive pulmonary disease, chronic obstructive pulmonary disease, emphysema, chronic bronchitis, bronchial asthma, bronchiectasis, bacterial pneumonia, viral and mycoplasmal pneumonia, lung abscess, pulmonary tuberculosis, diffuse interstitial diseases, pneumoconioses, sarcoidosis, idiopathic pulmonary fibrosis, desquamative interstitial pneumonitis, hypersensitivity pneumonitis, pulmonary eosinophilia bronchiolitis obliterans-organizing pneumonia, diffuse pulmonary hemorrhage syndromes, Goodpasture's syndromes, idiopathic pulmonary hemosiderosis, pulmonary involvement in collagen-vascular disorders, pulmonary alveolar proteinosis, lung tumors, inflammatory and noninflammatory pleural effusions, pneumothorax, and pleural tumors; neurological disorders such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease; prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome; fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal

hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis; inherited, metabolic, endocrine, and toxic myopathies; myasthenia gravis, periodic paralysis; mental disorders including mood, anxiety, and schizophrenic disorders; akathisia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, and Tourette's disorder; reproductive disorders such as disorders of prolactin production; infertility, including tubal disease, ovulatory defects, and endometriosis; disruptions of the estrous cycle, disruptions of the menstrual cycle, polycystic ovary syndrome, ovarian hyperstimulation syndrome, endometrial and ovarian tumors, uterine fibroids, autoimmune disorders, ectopic pregnancies, and teratogenesis; cancer of the breast, fibrocystic breast disease, and galactorrhea; disruptions of spermatogenesis, abnormal sperm physiology, cancer of the testis, cancer of the prostate, benign prostatic hyperplasia, prostatitis, Peyronie's disease, carcinoma of the male breast, and gynecomastia; and developmental disorders, such as renal tubular acidosis, anemia, Cushing's syndrome, achondroplastic dwarfism, Duchenne and Becker muscular dystrophy, epilepsy, gonadal dysgenesis, WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, and mental retardation), Smith-Magenis syndrome, myelodysplastic syndrome, hereditary mucoepithelial dysplasia, hereditary keratodermas, hereditary neuropathies such as Charcot-Marie-Tooth disease and neurofibromatosis, hypothyroidism, hydrocephalus, seizure disorders such as Sydenham's chorea and cerebral palsy, spina bifida, anencephaly, craniorachischisis, congenital glaucoma, cataract, and sensorineural hearing loss. The polynucleotide sequences encoding HSPP may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered HSPP expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, the nucleotide sequences encoding HSPP may be useful in assays that detect the presence of associated disorders, particularly those mentioned above. The nucleotide sequences encoding HSPP may be labeled by standard methods and added

to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantitated and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence  
5 of altered levels of nucleotide sequences encoding HSPP in the sample indicates the presence of the associated disorder. Such assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with  
10 expression of HSPP, a normal or standard profile for expression is established. This may be accomplished by combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding HSPP, under conditions suitable for hybridization or amplification. Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an  
15 experiment in which a known amount of a substantially purified polynucleotide is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated,  
20 hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either  
25 under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of  
30 the cancer.

Additional diagnostic uses for oligonucleotides designed from the sequences encoding HSPP may involve the use of PCR. These oligomers may be chemically

synthesized, generated enzymatically, or produced in vitro. Oligomers will preferably contain a fragment of a polynucleotide encoding HSPP, or a fragment of a polynucleotide complementary to the polynucleotide encoding HSPP, and will be employed under optimized conditions for identification of a specific gene or condition. Oligomers may  
5 also be employed under less stringent conditions for detection or quantitation of closely related DNA or RNA sequences.

Methods which may also be used to quantitate the expression of HSPP include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves. (See, e.g., Melby, P.C. et al. (1993) J.  
10 Immunol. Methods 159:235-244; Duplaa, C. et al. (1993) Anal. Biochem. 212:229-236.) The speed of quantitation of multiple samples may be accelerated by running the assay in an ELISA format where the oligomer of interest is presented in various dilutions and a spectrophotometric or colorimetric response gives rapid quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of  
15 the polynucleotide sequences described herein may be used as targets in a microarray. The microarray can be used to monitor the expression level of large numbers of genes simultaneously and to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, and to develop and monitor the activities of therapeutic  
20 agents.

Microarrays may be prepared, used, and analyzed using methods known in the art. (See, e.g., Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl. Acad. Sci. 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al.  
25 (1997) Proc. Natl. Acad. Sci. 94:2150-2155; and Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662.)

In another embodiment of the invention, nucleic acid sequences encoding HSPP may be used to generate hybridization probes useful in mapping the naturally occurring genomic sequence. The sequences may be mapped to a particular chromosome, to a  
30 specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs), yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single chromosome cDNA libraries.



(See, e.g., Harrington, J.J. et al. (1997) Nat Genet. 15:345-355; Price, C.M. (1993) Blood Rev. 7:127-134; and Trask, B.J. (1991) Trends Genet. 7:149-154.)

Fluorescent in situ hybridization (FISH) may be correlated with other physical chromosome mapping techniques and genetic map data. (See, e.g., Heinz-Ulrich, et al. 5 (1995) in Meyers, supra, pp. 965-968.) Examples of genetic map data can be found in various scientific journals or at the Online Mendelian Inheritance in Man (OMIM) site. Correlation between the location of the gene encoding HSPP on a physical chromosomal map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder. The nucleotide sequences of the invention 10 may be used to detect differences in gene sequences among normal, carrier, and affected individuals.

In situ hybridization of chromosomal preparations and physical mapping techniques, such as linkage analysis using established chromosomal markers, may be used for extending genetic maps. Often the placement of a gene on the chromosome of another 15 mammalian species, such as mouse, may reveal associated markers even if the number or arm of a particular human chromosome is not known. New sequences can be assigned to chromosomal arms by physical mapping. This provides valuable information to investigators searching for disease genes using positional cloning or other gene discovery techniques. Once the disease or syndrome has been crudely localized by genetic linkage to 20 a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23, any sequences mapping to that area may represent associated or regulatory genes for further investigation. (See, e.g., Gatti, R.A. et al. (1988) Nature 336:577-580.) The nucleotide sequence of the subject invention may also be used to detect differences in the chromosomal location due to translocation, inversion, etc., among normal, carrier, or affected individuals.

25 In another embodiment of the invention, HSPP, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes between HSPP and the agent being 30 tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest. (See, e.g., Geysen,

et al. (1984) PCT application WO84/03564.) In this method, large numbers of different small test compounds are synthesized on a solid substrate. The test compounds are reacted with HSPP, or fragments thereof, and washed. Bound HSPP is then detected by methods well known in the art. Purified HSPP can also be coated directly onto plates for use in the  
5   aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

In another embodiment, one may use competitive drug screening assays in which neutralizing antibodies capable of binding HSPP specifically compete with a test compound for binding HSPP. In this manner, antibodies can be used to detect the  
10   presence of any peptide which shares one or more antigenic determinants with HSPP.

In additional embodiments, the nucleotide sequences which encode HSPP may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely on properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair  
15   interactions.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

20    The disclosures of all applications, patents, and publications, mentioned above and below, in particular US Ser. No. 60/090,762, US Ser. No. 60/094,983, US Ser. No. 60/102,686, and US Ser. No. 60/112,129, are hereby expressly incorporated by reference.

## EXAMPLES

### 25   I.    Construction of cDNA Libraries

RNA was purchased from Clontech or isolated from tissues described in Table 4. Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed in phenol or in a suitable mixture of denaturants, such as TRIZOL (Life Technologies), a monophasic solution of phenol and guanidine  
30   isothiocyanate. The resulting lysates were centrifuged over CsCl cushions or extracted with chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA purity. In some cases, RNA was treated with DNase. For most libraries, poly(A+) RNA was isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN, Valencia CA), or an OLIGOTEX mRNA  
5 purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

In some cases, Stratagene was provided with RNA and constructed the corresponding cDNA libraries. Otherwise, cDNA was synthesized and cDNA libraries  
10 were constructed with the UNIZAP vector system (Stratagene) or SUPERScript plasmid system (Life Technologies), using the recommended procedures or similar methods known in the art. (See, e.g., Ausubel, 1997, supra, units 5.1-6.6). Reverse transcription was initiated using oligo d(T) or random primers. Synthetic oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA was digested with the appropriate  
15 restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000, SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Pharmacia Biotech) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g., PBLUESCRIPT plasmid (Stratagene), pSPORT1  
20 plasmid (Life Technologies), or pINCY (Incyte Pharmaceuticals, Palo Alto CA). Recombinant plasmids were transformed into competent *E. coli* cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5 $\alpha$ , DH10B, or ElectroMAX DH10B from Life Technologies.

## **II. Isolation of cDNA Clones**

25 Plasmids were recovered from host cells by in vivo excision, using the UNIZAP vector system (Stratagene) or cell lysis. Plasmids were purified using at least one of the following: a MAGIC or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plus Plasmid, QIAWELL 8 Ultra Plasmid purification systems or  
30 the REAL Prep 96 plasmid kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1 ml of distilled water and stored, with or without lyophilization, at 4°C.

Alternatively, plasmid DNA was amplified from host cell lysates using direct link PCR in a high-throughput format (Rao, V.B. (1994) Anal. Biochem. 216:1-14). Host cell lysis and thermal cycling steps were carried out in a single reaction mixture. Samples were processed and stored in 384-well plates, and the concentration of amplified plasmid DNA was quantified fluorometrically using PICOGREEN dye (Molecular Probes, Eugene  
5 OR) and a Fluoroskan II fluorescence scanner (Labsystems Oy, Helsinki, Finland).

### III. Sequencing and Analysis

The cDNAs were prepared for sequencing using the ABI CATALYST 800 (Perkin-Elmer) or the HYDRA microdispenser (Robbins Scientific) or MICROLAB 2200  
10 (Hamilton) systems in combination with the PTC-200 thermal cyclers (MJ Research). The cDNAs were sequenced using the ABI PRISM 373 or 377 sequencing systems (Perkin-Elmer) and standard ABI protocols, base calling software, and kits. In one alternative, cDNAs were sequenced using the MEGABACE 1000 DNA sequencing system (Molecular Dynamics). In another alternative, the cDNAs were amplified and sequenced  
15 using the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (Perkin-Elmer). In yet another alternative, cDNAs were sequenced using solutions and dyes from Amersham Pharmacia Biotech. Reading frames for the ESTs were determined using standard methods (reviewed in Ausubel, 1997, supra, unit 7.7). Some of the cDNA sequences were selected for extension using the techniques disclosed in Example V.

20 The polynucleotide sequences derived from cDNA, extension, and shotgun sequencing were assembled and analyzed using a combination of software programs which utilize algorithms well known to those skilled in the art. Table 5 summarizes the software programs, descriptions, references, and threshold parameters used. The first column of Table 5 shows the tools, programs, and algorithms used, the second column provides a  
25 brief description thereof, the third column presents the references which are incorporated by reference herein, and the fourth column presents, where applicable, the scores, probability values, and other parameters used to evaluate the strength of a match between two sequences (the higher the probability the greater the homology). Sequences were analyzed using MACDNASIS PRO software (Hitachi Software Engineering, South San  
30 Francisco CA) and LASERGENE software (DNASTAR).

The polynucleotide sequences were validated by removing vector, linker, and polyA sequences and by masking ambiguous bases, using algorithms and programs based

on BLAST, dynamic programing, and dinucleotide nearest neighbor analysis. The sequences were then queried against a selection of public databases such as GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS to acquire annotation, using programs based on BLAST, FASTA, and BLIMPS. The sequences were  
5 assembled into full length polynucleotide sequences using programs based on Phred, Phrap, and Consed, and were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length amino acid sequences, and these full length sequences were subsequently analyzed by querying against databases such as the  
10 GenBank databases (described above), SwissProt, BLOCKS, PRINTS, Prosite, and Hidden Markov Model (HMM)-based protein family databases such as PFAM. HMM is a probalistic approach which analyzes consensus primary structures of gene families. (See, e.g., Eddy, S.R. (1996) Cur. Opin. Str. Biol. 6:361-365.)

The programs described above for the assembly and analysis of full length  
15 polynucleotide and amino acid sequences were also used to identify polynucleotide sequence fragments from SEQ ID NO:135-268. Fragments from about 20 to about 4000 nucleotides which are useful in hybridization and amplification technologies were described in The Invention section above.

#### IV. Northern Analysis

20 Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound. (See, e.g., Sambrook, supra, ch. 7; Ausubel, 1995, supra, ch. 4 and 16.)

Analogous computer techniques applying BLAST were used to search for identical  
25 or related molecules in nucleotide databases such as GenBank or LIFESEQ database (Incyte Pharmaceuticals). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any particular match is categorized as exact or similar. The basis of the search is the product score, which is defined as:

30 
$$\frac{\% \text{ sequence identity} \times \% \text{ maximum BLAST score}}{100}$$

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. For example, with a product score of 40, the match will be exact within a 1% to 2% error, and, with a product score of 70, the match will be exact. Similar molecules are usually identified by selecting those which show product  
5 scores between 15 and 40, although lower scores may identify related molecules.

The results of northern analyses are reported as a percentage distribution of libraries in which the transcript encoding HSPP occurred. Analysis involved the categorization of cDNA libraries by organ/tissue and disease. The organ/tissue categories included cardiovascular, dermatologic, developmental, endocrine, gastrointestinal,  
10 hematopoietic/immune, musculoskeletal, nervous, reproductive, and urologic. The disease/condition categories included cancer, inflammation/trauma, cell proliferation, neurological, and pooled. For each category, the number of libraries expressing the sequence of interest was counted and divided by the total number of libraries across all categories. Percentage values of tissue-specific and disease- or condition-specific  
15 expression are reported in Table 3.

#### **V. Extension of HSPP Encoding Polynucleotides**

Full length nucleic acid sequences of SEQ ID NOs:135-229 were produced by extension of the component fragments described in Table 1, column 5, using oligonucleotide primers based on these fragments. For each nucleic acid sequence, one  
20 primer was synthesized to initiate extension of an antisense polynucleotide, and the other was synthesized to initiate extension of a sense polynucleotide. Primers were used to facilitate the extension of the known sequence "outward" generating amplicons containing new unknown nucleotide sequence for the region of interest. The initial primers were designed from the cDNA using OLIGO™ 4.06 (National Biosciences, Plymouth, MN), or  
25 another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

Selected human cDNA libraries (GIBCO BRL) were used to extend the sequence.  
30 If more than one extension is necessary or desired, additional sets of primers are designed to further extend the known region.

High fidelity amplification was obtained by following the instructions for the XL-PCR™ kit (The Perkin-Elmer Corp., Norwalk, CT) and thoroughly mixing the enzyme and reaction mix. PCR was performed using the PTC-200 thermal cycler (MJ Research, Inc., Watertown, MA), beginning with 40 pmol of each primer and the recommended

5 concentrations of all other components of the kit, with the following parameters:

|    |         |   |
|----|---------|---|
|    | Step 1  | 94° C for 1 min (initial denaturation)                |
|    | Step 2  | 65° C for 1 min                                       |
|    | Step 3  | 68° C for 6 min                                       |
|    | Step 4  | 94° C for 15 sec                                      |
| 10 | Step 5  | 65° C for 1 min                                       |
|    | Step 6  | 68° C for 7 min                                       |
|    | Step 7  | Repeat steps 4 through 6 for an additional 15 cycles  |
|    | Step 8  | 94° C for 15 sec                                      |
|    | Step 9  | 65° C for 1 min                                       |
| 15 | Step 10 | 68° C for 7:15 min                                    |
|    | Step 11 | Repeat steps 8 through 10 for an additional 12 cycles |
|    | Step 12 | 72° C for 8 min                                       |
|    | Step 13 | 4° C (and holding)                                    |

20 A 5  $\mu$ l to 10  $\mu$ l aliquot of the reaction mixture was analyzed by electrophoresis on a low concentration (about 0.6% to 0.8%) agarose mini-gel to determine which reactions were successful in extending the sequence. Bands thought to contain the largest products were excised from the gel, purified using QIAQUICK™ (QIAGEN Inc.), and trimmed of overhangs using Klenow enzyme to facilitate religation and cloning.

25 After ethanol precipitation, the products were redissolved in 13  $\mu$ l of ligation buffer, 1  $\mu$ l T4-DNA ligase (15 units) and 1  $\mu$ l T4 polynucleotide kinase were added, and the mixture was incubated at room temperature for 2 to 3 hours, or overnight at 16° C. Competent *E. coli* cells (in 40  $\mu$ l of appropriate media) were transformed with 3  $\mu$ l of ligation mixture and cultured in 80  $\mu$ l of SOC medium. (See, e.g., Sambrook, *supra*,  
 30 Appendix A, p. 2.) After incubation for one hour at 37° C, the *E. coli* mixture was plated on Luria Bertani (LB) agar (See, e.g., Sambrook, *supra*, Appendix A, p. 1) containing carbenicillin (2x carb). The following day, several colonies were randomly picked from each plate and cultured in 150  $\mu$ l of liquid LB/2x carb medium placed in an individual well of an appropriate commercially-available sterile 96-well microtiter plate. The  
 35 following day, 5  $\mu$ l of each overnight culture was transferred into a non-sterile 96-well plate and, after dilution 1:10 with water, 5  $\mu$ l from each sample was transferred into a PCR array.

For PCR amplification, 18  $\mu$ l of concentrated PCR reaction mix (3.3x) containing 4 units of rTth DNA polymerase, a vector primer, and one or both of the gene specific primers used for the extension reaction were added to each well. Amplification was performed using the following conditions:

|    |        |  |
|----|--------|--|
| 5  | Step 1 | 94° C for 60 sec                                     |
|    | Step 2 | 94° C for 20 sec                                     |
|    | Step 3 | 55° C for 30 sec                                     |
|    | Step 4 | 72° C for 90 sec                                     |
|    | Step 5 | Repeat steps 2 through 4 for an additional 29 cycles |
| 10 | Step 6 | 72° C for 180 sec                                    |
|    | Step 7 | 4° C (and holding)                                   |

Aliquots of the PCR reactions were run on agarose gels together with molecular weight markers. The sizes of the PCR products were compared to the original partial  
15 cDNAs, and appropriate clones were selected, ligated into plasmid, and sequenced.

The full length nucleic acid sequences of SEQ ID NO:230-268 were produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the other primer, to initiate 3' extension of the known  
20 fragment. The initial primers were designed using OLIGO 4.06 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

25 Selected human cDNA libraries were used to extend the sequence. If more than one extension was necessary or desired, additional or nested sets of primers were designed.

High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer,  
30 reaction buffer containing  $Mg^{2+}$ ,  $(NH_4)_2SO_4$ , and  $\beta$ -mercaptoethanol, Taq DNA polymerase (Amersham Pharmacia Biotech), ELONGASE enzyme (Life Technologies), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7:  
35 storage at 4°C. In the alternative, the parameters for primer pair T7 and SK+ were as



follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C.

The concentration of DNA in each well was determined by dispensing 100 µl  
5 PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene  
OR) dissolved in 1X TE and 0.5 µl of undiluted PCR product into each well of an opaque  
fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent.  
The plate was scanned in a Fluoroskan II (Labsystems Oy, Helsinki, Finland) to measure  
the fluorescence of the sample and to quantify the concentration of DNA. A 5 µl to 10 µl  
10 aliquot of the reaction mixture was analyzed by electrophoresis on a 1 % agarose mini-gel  
to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well  
plates, digested with CviJI cholera virus endonuclease (Molecular Biology Research,  
Madison WI), and sonicated or sheared prior to religation into pUC 18 vector (Amersham  
15 Pharmacia Biotech). For shotgun sequencing, the digested nucleotides were separated on  
low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested  
with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England  
Biolabs, Beverly MA) into pUC 18 vector (Amersham Pharmacia Biotech), treated with  
Pfu DNA polymerase (Stratagene) to fill-in restriction site overhangs, and transfected into  
20 competent *E. coli* cells. Transformed cells were selected on antibiotic-containing media,  
individual colonies were picked and cultured overnight at 37°C in 384-well plates in  
LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA  
polymerase (Amersham Pharmacia Biotech) and Pfu DNA polymerase (Stratagene) with  
25 the following parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min;  
Step 4: 72°C, 2 min; Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step  
7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as  
described above. Samples with low DNA recoveries were reamplified using the same  
conditions as described above. Samples were diluted with 20% dimethylsulphoxide (1:2,  
30 v/v), and sequenced using DYENAMIC energy transfer sequencing primers and the  
DYENAMIC DIRECT kit (Amersham Pharmacia Biotech) or the ABI PRISM BIGDYE  
Terminator cycle sequencing ready reaction kit (Perkin-Elmer).

In like manner, the nucleotide sequences of SEQ ID NO:135-268 are used to obtain 5' regulatory sequences using the procedure above, oligonucleotides designed for such extension, and an appropriate genomic library.

5 **VI. Labeling and Use of Individual Hybridization Probes**

Hybridization probes derived from SEQ ID NO:135-268 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20 base pairs, is specifically described, essentially the same procedure is used with larger nucleotide fragments. Oligonucleotides are designed using state-of-the-  
10 art software such as OLIGO 4.06 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250  $\mu$ Ci of [ $\gamma$ - $^{32}$ P] adenosine triphosphate (Amersham Pharmacia Biotech), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Pharmacia Biotech). An aliquot  
15 containing  $10^7$  counts per minute of the labeled probe is used in a typical membrane-based hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is  
20 carried out for 16 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature under increasingly stringent conditions up to 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. After XOMAT-AR film (Eastman Kodak, Rochester NY) is exposed to the blots to film for several hours, hybridization patterns are compared visually.

25 **VII. Microarrays**

A chemical coupling procedure and an ink jet device can be used to synthesize array elements on the surface of a substrate. (See, e.g., Baldeschweiler, supra.) An array analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using thermal, UV, chemical, or mechanical bonding procedures. A typical  
30 array may be produced by hand or using available methods and machines and contain any appropriate number of elements. After hybridization, nonhybridized probes are removed and a scanner used to determine the levels and patterns of fluorescence. The degree of

complementarity and the relative abundance of each probe which hybridizes to an element on the microarray may be assessed through analysis of the scanned images.

Full-length cDNAs, Expressed Sequence Tags (ESTs), or fragments thereof may comprise the elements of the microarray. Fragments suitable for hybridization can be  
5 selected using software well known in the art such as LASERGENE software (DNASTAR). Full-length cDNAs, ESTs, or fragments thereof corresponding to one of the nucleotide sequences of the present invention, or selected at random from a cDNA library relevant to the present invention, are arranged on an appropriate substrate, e.g., a glass  
10 slide. The cDNA is fixed to the slide using, e.g., UV cross-linking followed by thermal and chemical treatments and subsequent drying. (See, e.g., Schena, M. et al. (1995) Science 270:467-470; Shalon, D. et al. (1996) Genome Res. 6:639-645.) Fluorescent probes are prepared and used for hybridization to the elements on the substrate. The substrate is analyzed by procedures described above.

#### **VIII. Complementary Polynucleotides**

15 Sequences complementary to the HSPP-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring HSPP. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the  
20 coding sequence of HSPP. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the HSPP-encoding transcript.

#### **25 IX. Expression of HSPP**

Expression and purification of HSPP is achieved using bacterial or virus-based expression systems. For expression of HSPP in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels of cDNA transcription. Examples of such promoters include, but are  
30 not limited to, the *trp-lac* (*tac*) hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the *lac* operator regulatory element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3). Antibiotic resistant bacteria

express HSPP upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG).

Expression of HSPP in eukaryotic cells is achieved by infecting insect or mammalian cell lines with recombinant Autographica californica nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is replaced with cDNA encoding HSPP by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription. Recombinant baculovirus is used to infect Spodoptera frugiperda (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus. (See Engelhard, E. K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945.)

In most expression systems, HSPP is synthesized as a fusion protein with, e.g., glutathione S-transferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Pharmacia Biotech). Following purification, the GST moiety can be proteolytically cleaved from HSPP at specifically engineered sites. FLAG, an 8-amino acid peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel (1995, supra, ch 10 and 16). Purified HSPP obtained by these methods can be used directly in the following activity assay.

25

## **X. Demonstration of HSPP Activity**

### **HSPP-68**

HSPP-68 activity is measured by determining the potassium current using voltage clamp analysis on single Xenopus laevis oocytes injected with HSPP-68 cRNA. HSPP-68 cRNA is synthesized in vitro from linearized HSPP-68 encoding plasmids using the T7

RNA polymerase and injected into oocytes.. Injected oocytes are used two to four days after injection. In a 0.3 ml perfusion chamber, a single oocyte is impaled with two standard microelectrodes (1-2.5 M $\Omega$ ) filled with 3 M KCl. The oocyte is maintained under voltage clamp by using a Dagan TEV 200 amplifier, in buffer containing 96 mM NaCl, 2 mM KCl, 1.8 mM CaCl<sub>2</sub>, 2 mM MgCl<sub>2</sub>, 5 mM HEPES, pH 7.4 with NaOH.

Stimulation of the preparation, data acquisition, and analysis is performed using a computer. All experiments are performed at room temperature (21-22 °C). Following a depolarizing pulse, the characteristics of the resulting potassium current are measured via the recording electrode. The amount of potassium current that flows in response to a unit depolarization is proportional to the activity of HSPP-68 in the cell. (Duprat, F. et al. (1997) EMBO J. 16:5464-5471.)

#### HSPP-92

HSPP-92 protein phosphatase activity is measured by the hydrolysis of P-nitrophenyl phosphate (PNPP). HSPP-92 is incubated together with PNPP in HEPES buffer pH 7.5, in the presence of 0.1% b-mercaptoethanol at 37°C for 60 min. The reaction is stopped by the addition of 6 ml of 10 N NaOH and the increase in light absorbance at 410 nm resulting from the hydrolysis of PNPP is measured using a spectrophotometer. The increase in light absorbance is proportional to the activity of PP in the assay. (Diamond R.H. et al (1994) Mol Cell Biol 14:3752-62.)

Alternatively, HSPP, or biologically active fragments thereof, are labeled with <sup>125</sup>I Bolton-Hunter reagent. (See, e.g., Bolton et al. (1973) Biochem. J. 133:529.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled HSPP, washed, and any wells with labeled HSPP complex are assayed. Data obtained using different concentrations of HSPP are used to calculate values for the number, affinity, and association of HSPP with the candidate molecules.

Alternatively, an assay for HSPP activity measures the expression of HSPP on the cell surface. cDNA encoding HSPP is subcloned into an appropriate mammalian expression vector suitable for high levels of cDNA expression. The resulting construct is transfected into a nonhuman cell line such as NIH3T3. Cell surface proteins are labeled with biotin using methods known in the art. Immunoprecipitations are performed using HSPP-specific antibodies, and immunoprecipitated samples are analyzed using SDS-PAGE and immunoblotting techniques. The ratio of labeled immunoprecipitant to

unlabeled immunoprecipitant is proportional to the amount of HSPP expressed on the cell surface.

Alternatively, an assay for HSPP activity measures the amount of HSPP in secretory, membrane-bound organelles. Transfected cells as described above are harvested  
5 and lysed. The lysate is fractionated using methods known to those of skill in the art, for example, sucrose gradient ultracentrifugation. Such methods allow the isolation of subcellular components such as the Golgi apparatus, ER, small membrane-bound vesicles, and other secretory organelles. Immunoprecipitations from fractionated and total cell lysates are performed using HSPP-specific antibodies, and immunoprecipitated samples  
10 are analyzed using SDS-PAGE and immunoblotting techniques. The concentration of HSPP in secretory organelles relative to HSPP in total cell lysate is proportional to the amount of HSPP in transit through the secretory pathway.

#### **XI. Functional Assays**

HSPP function is assessed by expressing the sequences encoding HSPP at  
15 physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include pCMV SPORT (Life Technologies) and pCR3.1 (Invitrogen, Carlsbad CA), both of which contain the cytomegalovirus promoter. 5-10  $\mu$ g of recombinant vector are transiently transfected into a human cell line, preferably  
20 of endothelial or hematopoietic origin, using either liposome formulations or electroporation. 1-2  $\mu$ g of an additional plasmid containing sequences encoding a marker protein are co-transfected. Expression of a marker protein provides a means to distinguish transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent  
25 Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser optics-based technique, is used to identify transfected cells expressing GFP or CD64-GFP, and to evaluate properties, for example, their apoptotic state. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with cell death. These events include changes in nuclear DNA content as  
30 measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; down-regulation of DNA synthesis as measured by decrease in bromodeoxyuridine uptake; alterations in

expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M. G. (1994) Flow Cytometry, Oxford, New York

5 NY.

The influence of HSPP on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding HSPP and either CD64 or CD64-GFP. CD64 and CD64-GFP are expressed on the surface of transfected cells and bind to conserved regions of human immunoglobulin G (IgG). Transfected cells are efficiently  
10 separated from nontransfected cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding HSPP and other genes of interest can be analyzed by northern analysis or microarray techniques.

## 15 XII. Production of HSPP Specific Antibodies

HSPP substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) *Methods Enzymol.* 182:488-495), or other purification techniques, is used to immunize rabbits and to produce antibodies using standard protocols.

20 Alternatively, the HSPP amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art. (See, e.g., Ausubel,  
25 1995, supra, ch. 11.)

Typically, oligopeptides 15 residues in length are synthesized using an ABI 431A Peptide Synthesizer (Perkin-Elmer) using fmoc-chemistry and coupled to KLH (Sigma-Aldrich, St. Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase immunogenicity. (See, e.g., Ausubel, 1995, supra.) Rabbits are  
30 immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for antipeptide activity by, for example, binding the peptide to plastic,

blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

### **XIII. Purification of Naturally Occurring HSPP Using Specific Antibodies**

Naturally occurring or recombinant HSPP is substantially purified by

5 immunoaffinity chromatography using antibodies specific for HSPP. An immunoaffinity column is constructed by covalently coupling anti-HSPP antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

10 Media containing HSPP are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of HSPP (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/HSPP binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and HSPP is collected.

### **15 XIV. Identification of Molecules Which Interact with HSPP**

HSPP, or biologically active fragments thereof, are labeled with <sup>125</sup>I Bolton-Hunter reagent. (See, e.g., Bolton et al. (1973) Biochem. J. 133:529.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled HSPP, washed, and any wells with labeled HSPP complex are assayed. Data  
20 obtained using different concentrations of HSPP are used to calculate values for the number, affinity, and association of HSPP with the candidate molecules.

Various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with  
25 specific preferred embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the following claims.



TABLE I

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments  |
|-----------------------|--------------------------|----------|-----------|--|
| 1                     | 135                      | 443531   | MPHGNOT03 | 443531H1 (MPHGNOT03), 1406807F6 (LATRTUT02), 443531T6 (MPHGNOT03), SBBA00451F1, SBBA00676F1  |
| 2                     | 136                      | 632860   | NEUTGMT01 | 632860H1 (NEUTGMT01), 784715R3 (PROSNOT05), 509590H1 (MPHGNOT03)   |
| 3                     | 137                      | 670010   | CRBLNOT01 | 670010H1 (CRBLNOT01), 669971R1 (CRBLNOT01), 1553045F1 (BLADTUT04)  |
| 4                     | 138                      | 726498   | SYNOOAT01 | 726498H1 (SYNOOAT01), 726498R6 (SYNOOAT01), 866599R3 (BRAITUT03)   |
| 5                     | 139                      | 795064   | OVARNOT03 | 795064H1 (OVARNOT03), 4339458H1 (BRAUNOT02), 937605R3 (CERVNOT01), 2381151F6 (ISLTNOT01), 1466346F6 (PANCNUT02)  |
| 6                     | 140                      | 924925   | BRAINOT04 | 924925H1 (BRAINOT04), 3268330H1 (BRAINOT20), 759120R3 (BRAITUT02)  |
| 7                     | 141                      | 962390   | BRSTTUT03 | 962390H1 (BRSTTUT03), 1907958F6 (CONNTUT01), 023569F1 (ADENINB01), 167282F1 (LIVRNOT01), 1309211F1 (COLNFET02), SAUA00696F1, SAUA02860F1                                 |
| 8                     | 142                      | 1259405  | MENITUT03 | 1259405H1 (MENITUT03), 2472425H1 (THPINOT03), 774303R1 (COLNNOT05), 1520779F1 (BLADTUT04), 1693833F6 (COLNNOT23), 1831858T6.comp (THPIAZT01), 1527737T6.comp (UCMCL5T01) |
| 9                     | 143                      | 1297384  | BRSTNOT07 | 1297384H1 (BRSTNOT07), 1269310F6 (BRAINOT09), 1457367F1 (COLNFET02), 415587R1 (BRSTNOT01), SANA02967F1   |
| 10                    | 144                      | 1299627  | BRSTNOT07 | 1299627H1 (BRSTNOT07), 1359140F6 (LUNGNOT09), 1349224F1 (LATRTUT02), SBAA01431F1, SBAA02909F1, SBAA01156F1   |
| 11                    | 145                      | 1306026  | PLACNOT02 | 1306026H1 (PLACNOT02), 1464088R6 (PANCNOT04), SBAA02496F1, SBAA04303F1   |
| 12                    | 146                      | 1316219  | BLADTUT02 | 1316219H1 (BLADTUT02), 2458603F6 (ENDANOT01), 2504756T6 (CONUTUT01)  |
| 13                    | 147                      | 1329031  | PANCNOT07 | 1329031H1 (PANCNOT07), 1329031T6 (PANCNOT07), 1329031F6 (PANCNOT07)  |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments   |
|-----------------------|--------------------------|----------|-----------|---|
| 14                    | 148                      | 1483050  | CORPNOT02 | 1483050HI (CORPNOT02), 855049HI (NGANNOT01), 077017F1 (SYNORAB01), 1483050F6 (CORPNOT02), 1480024T6 (CORPNOT02), 1483050T6 (CORPNOT02), 759486R1 (BRAITUT02)  |
| 15                    | 149                      | 1514160  | PANCTUT01 | 1514160HI (PANCTUT01), 1866765T7 (SKINBIT01), 782676R1 (MYOMNOT01), 008055X4 (HMCINOT01), 008055X5 (HMCINOT01), 1866765F6 (SKINBIT01), SAOA03127F1  |
| 16                    | 150                      | 1603403  | LUNGNOT15 | 1603403HI (LUNGNOT15), 372910F1 (LUNGNOT02), 733299R7 (LUNGNOT03)   |
| 17                    | 151                      | 1652303  | PROSTUT08 | 1652303HI (PROSTUT08), 1671806HI (BLADNOT05), 1341743T1 (COLNTUT03), 3803812HI (BLADTUT03), 1878546F6 (LEUKNOT03), 1428640F1 (SINTBST01), 2058609R6 (OVARNOT03), 1331621F1 (PANCNOT07), 1306331T1 (PLACNOT02) |
| 18                    | 152                      | 1693358  | COLNNOT23 | 1693358HI (COLNNOT23), 2498265HI (ADRETUT05), 1867125F6 (SKINBIT01), 1693358T6 (COLNNOT23), 2245848R6 (HIPONON02)   |
| 19                    | 153                      | 1707711  | DUODNOT02 | 1707711HI (DUODNOT02), 1484609T1 (CORPNOT02), 1707711F6 (DUODNOT02), 1267959F1 (BRAINOT09), 1484609F1 (CORPNOT02), SAJA00930F1, SAJA01300R1, SAJA00999R1  |
| 20                    | 154                      | 1738735  | COLNNOT22 | 1738735HI (COLNNOT22), SAJA00944R1, SAJA00137F1, SAJA03629F1  |
| 21                    | 155                      | 1749147  | STOMTUT02 | 1749147HI (STOMTUT02), 1749147F6 (STOMTUT02), 1749147T6 (STOMTUT02)   |
| 22                    | 156                      | 1817722  | PROSNOT20 | 1817722HI (PROSNOT20), 2011085HI (TESTNOT03)  |
| 23                    | 157                      | 1831290  | THPIAZT01 | 1831290HI (THPIAZT01), 3473958HI (LUNGNOT27), 1972268F6 (UCMCL5T01), 1301277F1 (BRSTNOT07), 1521574F1 (BLADTUT04), 1561690T6 (SPLNNOT04), 891461R1 (STOMTUT01)  |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments  |
|-----------------------|--------------------------|----------|-----------|--|
| 24                    | 158                      | 1831477  | THP1AZT01 | 1831477H1 (THP1AZT01), 1582867H1 (DUODNOT01), 1336769T1 (COLNNOT13), 1933092H1 (COLNNOT16), 1519909F1 (BLADTUT04), 1220946H1 (NEUTGMT01), 809556T1 (LUNGNOT04), 1217559T1 (NEUTGMT01), 1309225F1 (COLNFET02) |
| 25                    | 159                      | 1841607  | COLNNOT07 | 1841607H1 (COLNNOT07), SBHA03588F1   |
| 26                    | 160                      | 1852391  | LUNGFET03 | 1852391H1 (LUNGFET03), 734140H1 (TONSNOT01), 1852391F6 (LUNGFET03)   |
| 27                    | 161                      | 1854555  | HNT3AZT01 | 1854555H1 (HNT3AZT01), 2511711H1 (CONUTUT01), 782453R1 (MYOMNOT01), 1854555F6 (HNT3AZT01), 1840675T6 (COLNNOT07), 2109736H1 (BRAITUT03)  |
| 28                    | 162                      | 1855755  | PROSNOT18 | 1855755H1 (PROSNOT18), 3040236H1 (BRSTNOT16), 1283207F1 (COLNNOT16), 833763T1 (PROSNOT07), 1920926R6 (BRSTTUT01)   |
| 29                    | 163                      | 1861434  | PROSNOT19 | 1861434H1 (PROSNOT19), 980291R1 (TONGTUT01), 1861434T6 (PROSNOT19), SARA01525F1, SARA02548F1   |
| 30                    | 164                      | 1872334  | LEUKNOT02 | 1872334H1 (LEUKNOT02), 1872334F6 (LEUKNOT02), SBGA03684F1  |
| 31                    | 165                      | 1877230  | LEUKNOT03 | 1877230H1 (LEUKNOT03), 2519841H1 (BRAITUT21), 1877230T6 (LEUKNOT03), 1254693F1 (LUNGFET03), 077020R1 (SYNORAB01), 1232336F1 (LUNGFET03), 1004952R6 (BRSTNOT03), SARA01879F1, SARA02654F1                     |
| 32                    | 166                      | 1877885  | LEUKNOT03 | 1877885H1 (LEUKNOT03), 508020F1 (TMLR3DT01), 2751126R6 (THP1AZS08), SARA02571F1  |
| 33                    | 167                      | 1889269  | BLADTUT07 | 1889269H1 (BLADTUT07), 1915551H1 (PROSTUT04), 629493X12 (KIDNNOT05), 1441289F1 (THYRNOT03), 1215274X34F1 (BRSTTUT01), 1818447F6 (PROSNOT20), 1208463R1 (BRSTNOT02)   |
| 34                    | 168                      | 1890243  | BLADTUT07 | 1890243H1 (BLADTUT07), SARA01884F1, SARA00046F1, SARA03294F1, SARA02790F1  |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments  |
|-----------------------|--------------------------|----------|-----------|--|
| 35                    | 169                      | 1900433  | BLADTUT06 | 1900433HI (BLADTUT06), SATA00396F1, SATA02742F1  |
| 36                    | 170                      | 1909441  | CONNTUT01 | 1909441HI (CONNTUT01), 1398811F1 (BRAITUT08), 3039939HI (BRSTNOT16), 3324740HI (PTHYNOT03), 1442131F6 (THYRNOT03), 2254056HI (OVRTUT01), 2199453T6 (SPLNFET02), 1692610F6 (COLNNOT23), 1698531HI (BLADTUT05) |
| 37                    | 171                      | 1932226  | COLNNOT16 | 1932226HI (COLNNOT16), 2320569HI (OVARNOT02), 1932226F6 (COLNNOT16), 2469455T6 (THP1NOT03), 2469455F6 (THP1NOT03), 1907140F6 (OVARNOT07), SATA02592F1  |
| 38                    | 172                      | 1932647  | COLNNOT16 | 1932647HI (COLNNOT16), 1492745T1 (PROSNON01), 1492745HI (PROSNON01), SASA02355F1, SASA00117F1, SASA00192F1   |
| 39                    | 173                      | 2124245  | BRSTNOT07 | 2124245HI (BRSTNOT07), 1235393F1 (LUNGFEF03), 1402264F6 (LATRTUT02), 1303990F1 (PLACNOT02), 1402264T6 (LATRTUT02)  |
| 40                    | 174                      | 2132626  | OVARNOT03 | 2132626HI (OVARNOT03), 1723432T6 (BLADNOT06), 2132626R6 (OVARNOT03), 1736723T6 (COLNNOT22), 1504738F1 (BRAITUT07)  |
| 41                    | 175                      | 2280639  | PROSNON01 | 2280639HI (PROSNON01), 1435330HI (PANCNOT08), 1377560F6 (LUNGNOT10)  |
| 42                    | 176                      | 2292356  | BRAINON01 | 2292356HI (BRAINON01), 4086827HI (LIVRNOT06), 1754442F6 (LIVRTUT01), 3571126HI (HEAPNOT01), 1601305F6 (BLADNOT03)  |
| 43                    | 177                      | 2349310  | COLSUCT01 | 2349310HI (COLSUCT01), 2349310T6 (COLSUCT01)   |
| 44                    | 178                      | 2373227  | ADRENOT07 | 2373227HI (ADRENOT07), 3316444HI (PROSBPT03), 302685R6 (TESTNOT04), SASA02181F1, SASA01923F1, SASA03516F1  |
| 45                    | 179                      | 2457682  | ENDANOT01 | 2457682HI (ENDANOT01), 2457682F6 (ENDANOT01)   |
| 46                    | 180                      | 2480426  | SMCANOT01 | 2480426HI (SMCANOT01), 2480426F6 (SMCANOT01)   |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments   |
|-----------------------|--------------------------|----------|-----------|---|
| 47                    | 181                      | 2503743  | CONUTUT01 | 2503743HI (CONUTUT01), 1853909HI (HNT3AZT01), 1517619F1 (PANCUTUT01), 1467896F6 (PANCUTUT02), 490031F1 (HNT2AGT01), 1208654R1 (BRSTNOT02), 880544R1 (THYRN0T02)                     |
| 48                    | 182                      | 2537684  | BONRTUT01 | 2537684HI (BONRTUT01), 2005493HI (TESTNOT03), 730969HI (LUNGNOT03), 2537601F6 (BONRTUT01), 916487HI (BRSTNOT04), 996135R1 (KIDNTUT01), 1920738R6 (BRSTTUT01), 1957710F6 (CONNNOT01) |
| 49                    | 183                      | 2593853  | OVARTUT02 | 2593853HI (OVARTUT02), 807497HI (STOMNOT02), 914020R6 (STOMNOT02), 889992R1 (STOMTUT01)   |
| 50                    | 184                      | 2622354  | KERANOT02 | 2622354HI (KERANOT02), 2623992HI (KERANOT02), 1556510F6 (BLADTUT04)   |
| 51                    | 185                      | 2641377  | LUNGTUT08 | 2641377HI (LUNGTUT08), 4341415H2 (BRAUNOT02), SBDA07049F3   |
| 52                    | 186                      | 2674857  | KIDNNOT19 | 2674857HI (KIDNNOT19), 1872373HI (LEUKNOT02), 470512R6 (MMLRIDT01), 1728547HI (PROSNOT14), 3013651F6 (MUSCNOT07), SBDA01366F1, SBDA00694F1  |
| 53                    | 187                      | 2758485  | THPIAZS08 | 2758485HI (THPIAZS08), 3097533HI (CERVNOT03), 1578959F6 (DUODNOT01)   |
| 54                    | 188                      | 2763296  | BRSTNOT12 | 2763296HI (BRSTNOT12), 3486025F6 (KIDNNOT31), SBDA07002F3   |
| 55                    | 189                      | 2779436  | OVARTUT03 | 2779436HI (OVARTUT03), 2779436F6 (OVARTUT03), SBDA07009F3   |
| 56                    | 190                      | 2808528  | BLADTUT08 | 2808528HI (BLADTUT08), 2611513F6 (THYMN0T04), SBDA07021T3   |
| 57                    | 191                      | 2809230  | BLADTUT08 | 2809230HI (BLADTUT08), 2213849HI (SINTFET03), 711706R6 (SYNORAT04), 958323R1 (KIDNNOT05), 030732F1 (THPINOB01)  |
| 58                    | 192                      | 2816821  | BRSTNOT14 | 2816821HI (BRSTNOT14), 3746964HI (THYMN0T08), 2816821F6 (BRSTNOT14), 948722T6 (PANCNOT05), 807947R6 (STOMNOT02)   |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments   |
|-----------------------|--------------------------|----------|-----------|---|
| 59                    | 193                      | 2817268  | BRSTNOT14 | 2817268HI (BRSTNOT14), 3591308HI (293TF5T01), 419522RI (BRSTNOT01), 2073028F6 (ISLTNOT01), 1308781F6 (COLNFET02)  |
| 60                    | 194                      | 2923165  | SININOT04 | 2923165HI (SININOT04), 2011630HI (TESTNOT03), 1457250F1 (COLNFET02), 754668RI (BRAITUT02), 1406510F6 (LATRTUT02)  |
| 61                    | 195                      | 2949822  | KIDNFET01 | 2949822HI (KIDNFET01), SBDA07078F3  |
| 62                    | 196                      | 2992192  | KIDNFET02 | 2992192HI (KIDNFET02), 2534324H2 (BRAINOT18), 2815255T6 (OVARNOT10), 1551107T6 (PROSNOT06), 1551107R6 (PROSNOT06)   |
| 63                    | 197                      | 2992458  | KIDNFET02 | 2992458HI (KIDNFET02), 2618951HI (GBLANOT01), 1479252F1 (CORPNOT02), 1879054HI (LEUKNOT03), 1879054F6 (LEUKNOT03), 2215240HI (SINTFET03), 1535968T1 (SPLNNOT04)   |
| 64                    | 198                      | 3044710  | HEAANOT01 | 3044710HI (HEAANOT01), 3741773HI (MENTNOT01), 859906X42CI (BRAITUT03), 1534347F1 (SPLNNOT04), 1421122F1 (KIDNNOT09), 1303865F1 (PLACNOT02), 1704452F6 (DUODNOT02), 1251642F1 (LUNGFET03), 1781694R6 (PGANNON02) |
| 65                    | 199                      | 3120415  | LUNGTUT13 | 3120415HI (LUNGTUT13), 1360123T1 (LUNGNOT12), 1375015HI (LUNGNOT10)   |
| 66                    | 200                      | 126758   | LUNGNOT01 | 126758HI (LUNGNOT01), 126758X11 (LUNGNOT01), 811864T1 (LUNGNOT04)   |
| 67                    | 201                      | 674760   | CRBLNOT01 | 674760HI (CRBLNOT01), 3253976HI (OVRTUN01), SAUA03387F1   |
| 68                    | 202                      | 1229438  | BRAITUT01 | 1229438HI (BRAITUT01), 1230616HI (BRAITUT01), 1461187RI (PANCNOT04), 2493039HI (ADRETUT05), 2891628HI (LUNGFET04)   |
| 69                    | 203                      | 1236935  | LUNGFET03 | 1236935HI (LUNGFET03), SBAA00983F1, SBAA02057F1, SBAA00170F1  |
| 70                    | 204                      | 1359283  | LUNGNOT12 | 1359283HI (LUNGNOT12), SBAA01213F1, SBAA03934F1   |
| 71                    | 205                      | 1450703  | PENITUT01 | 551298F1 (BEPINOT01), 551298RI (BEPINOT01), 1450703HI (PENITUT01), 2748715HI (LUNGTUT11)  |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments   |
|-----------------------|--------------------------|----------|-----------|---|
| 72                    | 206                      | 1910668  | CONNTUT01 | 1269346H1 (BRAINOT09), 1380872F1 (BRAITUT08), 1910668F6 (CONNTUT01), 1910668H1 (CONNTUT01), SATA02800F1, SATA03799F1, SARA02035F1       |
| 73                    | 207                      | 1955143  | CONNNOT01 | 1955143F6 (CONNNOT01), 1955143H1 (CONNNOT01)  |
| 74                    | 208                      | 1961637  | BRSTNOT04 | 867025H1 (BRAITUT03), 1961637H1 (BRSTNOT04), 2809064T6 (BLADTUT08), 2938714H1 (THYMFET02), 2956402H1 (KIDNFET01), 3808735T6 (CONTTUT01) |
| 75                    | 209                      | 1990762  | CORPNOT02 | 1990762H1 (CORPNOT02), 1990762T3 (CORPNOT02), SBGA04911F1, SBGA01201F1, SBGA02205F1   |
| 76                    | 210                      | 1994131  | CORPNOT02 | 1994131H1 (CORPNOT02), 2645984F6 (OVARUT04)   |
| 77                    | 211                      | 1997745  | BRSTTUT03 | 1752307F6 (LIVRTUT01), 1853730H1 (HNT3AZT01), 1997745H1 (BRSTTUT03), SAZA00953F1  |
| 78                    | 212                      | 2009035  | TESTNOT03 | 2009035H1 (TESTNOT03), 2009035R6 (TESTNOT03)  |
| 79                    | 213                      | 2009152  | TESTNOT03 | 2009152H1 (TESTNOT03), 2009152R6 (TESTNOT03), 2783263H1 (BRSTNOT13)   |
| 80                    | 214                      | 2061752  | OVARNOT03 | 2061752H1 (OVARNOT03), 2061752T6 (OVARNOT03), 2732805H1 (OVARUT04), SAZA01310F1, SAZA00830F1  |
| 81                    | 215                      | 2061933  | OVARNOT03 | 046580R1 (CORNNOT01), 746061R1 (BRAITUT01), 826996R1 (PROSNOT06), 2061933H1 (OVARNOT03)   |
| 82                    | 216                      | 2081422  | UTRSNOT08 | 2081422F6 (UTRSNOT08), 2081422H1 (UTRSNOT08), SBGA04793F1, SBGA05657F1, SBDA00065F1   |
| 83                    | 217                      | 2101278  | BRAITUT02 | 2101278H1 (BRAITUT02), SAXA00399F1, SAXA01284F1, SAXA01227F1  |
| 84                    | 218                      | 2121353  | BRSTNOT07 | 341437H1 (NEUTFM01), 687136H1 (UTRSNOT02), 2121353H1 (BRSTNOT07), SASA01311F1   |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments   |
|-----------------------|--------------------------|----------|-----------|---|
| 85                    | 219                      | 2241736  | PANCTUT02 | 833263HI (PROSTUT04), 2241736HI (PANCTUT02), SAZA01148FI,<br>SASA03299FI, SASA01349FI   |
| 86                    | 220                      | 2271935  | PROSNON01 | 2271935HI (PROSNON01), 2276774HI (PROSNON01), 2760171T6<br>(THPIAZS08)  |
| 87                    | 221                      | 2295344  | BRSTNOT05 | 2295344HI (BRSTNOT05), 3288561F6 (BONRFET01), SBGA01801FI   |
| 88                    | 222                      | 2303994  | BRSTNOT05 | 905482T1 (COLNNOT08), 1858636F6 (PROSNOT18), 2303994HI (BRSTNOT05)  |
| 89                    | 223                      | 2497805  | ADRETUT05 | 2497805F6 (ADRETUT05), 2497805HI (ADRETUT05)  |
| 90                    | 224                      | 2646362  | LUNGTUT11 | 1754702HI (LIVRTUT01), 2640776T6 (LUNGTUT08), 2646362HI<br>(LUNGTUT11), 3356773HI (PROSTUT16)   |
| 91                    | 225                      | 2657146  | LUNGTUT09 | 2657146F6 (LUNGTUT09), 2657146HI (LUNGTUT09)  |
| 92                    | 226                      | 2755786  | THPIAZS08 | 288436R1 (EOSIHET02), 1252824F6 (LUNGFET03), 1305549HI (PLACNOT02),<br>1364975R1 (SCORNON02), 2018293HI (THPINOT01), 2047320HI<br>(THPIT7T01), 2184537F6 (SININOT01), 2755786HI (THPIAZS08), 4111022HI<br>(PROSBPT07) |
| 93                    | 227                      | 2831245  | TLYMNOT03 | 2831245HI (TLYMNOT03), SBMA01396FI  |
| 94                    | 228                      | 3116250  | LUNGTUT13 | 126263FI (LUNGNOT01), 2729942HI (OVRTUT04), 3116250HI<br>(LUNGTUT13)  |
| 95                    | 229                      | 3129630  | LUNGTUT12 | 3129630F6 (LUNGTUT12), 3129630HI (LUNGTUT12), SBDA06436FI   |
| 96                    | 230                      | 007632   | HMCINOT01 | 007632HI (HMCINOT01), 007632R6 (HMCINOT01), 007632T6 (HMCINOT01)  |
| 97                    | 231                      | 1236968  | LUNGFET03 | 1236968HI (LUNGFET03), SBAA02713FI, SBAA03203FI, SBAA04196FI  |
| 98                    | 232                      | 1334153  | COLNNOT13 | 776410R1 (COLNNOT05), 1334153HI (COLNNOT13), 1334153TI<br>(COLNNOT13), 1800085F6 (COLNNOT27), 2701948HI (OVRTUT10)  |



TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments   |
|-----------------------|--------------------------|----------|-----------|---|
| 99                    | 233                      | 1396975  | BRAITUT08 | 864113HI (BRAITUT03), 876139RI (LUNGAST01), 1268313F1 (BRAINOT09),<br>1351348T1 (LATRTUT02), 1396975HI (BRAITUT08), 1485768F6<br>(CORPNOT02), 1815364F6 (PROSNOT20)         |
| 100                   | 234                      | 1501749  | SINTBST01 | 079080RI (SYNORAB01), 1501749HI (SINTBST01), 1724970HI (PROSNOT14)  |
| 101                   | 235                      | 1575240  | LNODNOT03 | 081858RI (SYNORAB01), 1575240HI (LNODNOT03), 3451462R6<br>(UTRSNON03)   |
| 102                   | 236                      | 1647884  | PROSTUT09 | 1647884HI (PROSTUT09), 1647884T6 (PROSTUT09), 3998922R6 (HNT2AZS07)   |
| 103                   | 237                      | 1661144  | BRSTNOT09 | 720941X17 (SYNOOAT01), 1661144HI (BRSTNOT09), 2181782HI (SININOT01)   |
| 104                   | 238                      | 1685409  | PROSNOT15 | 755203RI (BRAITUT02), 1226185T1 (COLNNOT01), 1300837F1 (BRSTNOT07),<br>1685409HI (PROSNOT15), 1705256HI (DUODNOT02)   |
| 105                   | 239                      | 1731419  | BRSTTUT08 | 1731419HI (BRSTTUT08), 1731419X319T3 (BRSTTUT08), 1731419X322F1<br>(BRSTTUT08), 1731419X326F1 (BRSTTUT08), 1731419X329F1 (BRSTTUT08),<br>1733786F6 (BRSTTUT08), SZAH01494F1 |
| 106                   | 240                      | 2650265  | BRSTNOT14 | 1680316T6 (STOMFET01), 2650265HI (BRSTNOT14), 2650265T6<br>(BRSTNOT14), 2760588R6 (BRAINOS12)   |
| 107                   | 241                      | 2677129  | KIDNNOT19 | 1592129HI (CARGNOT01), 2645962HI (OVARUT04), 2677129F6<br>(KIDNNOT19), 2677129HI (KIDNNOT19), 2910973HI (KIDNNOT15),<br>4571722HI (PROSTMT02), 4906791H2 (TLYMNOT08)        |
| 108                   | 242                      | 3151073  | ADRENON04 | 3150857T6 (ADRENON04), 3151073HI (ADRENON04), 3151073R6<br>(ADRENON04)  |
| 109                   | 243                      | 3170095  | BRSTNOT18 | 3170095F6 (BRSTNOT18), 3170095HI (BRSTNOT18)  |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments  |
|-----------------------|--------------------------|----------|-----------|--|
| 110                   | 244                      | 3475168  | LUNGNOT27 | 079680F1 (SYNORAB01), 443811T6 (MPHGN0T03), 1509356T6 (LUNGNOT14), 1873596F6 (LEUKNOT02), 2440867H1 (EOSITXT01), 3475168H1 (LUNGNOT27)   |
| 111                   | 245                      | 3836893  | DENDTNT01 | 446637H1 (MPHGN0T03), 1219376R6 (NEUTGMT01), 3735467F6 (SMCCN0S01), 3735467T6 (SMCCN0S01), 3836893H1 (DENDTNT01)   |
| 112                   | 246                      | 4072159  | KIDNNOT26 | 2129415T6 (KIDNNOT05), 4072159F6 (KIDNNOT26), 4072159H1 (KIDNNOT26)  |
| 113                   | 247                      | 1003916  | BRSTNOT03 | 620937R6 (PGANN0T01), 1003916H1 and 1003916R6 (BRSTNOT03), 1413623H1 (BRAINT02), 1435945F1 (PANCNOT08), 1479127F1 (CORPNOT02), 1969146R6 (BRSTNOT04), 2517587F6 (BRAITUT21), 2967848H1 (SCORNOT04)                                     |
| 114                   | 248                      | 2093492  | PANCNOT04 | 489651H1 (HNT2AGT01), 1265353T1 (SYNORAT05), 1431505R6 (BEPINON01), 1605237F6 (LUNGNOT15), 2093492H1 and 2093492T6 (PANCNOT04), 4195560H1 (COLITUT02)  |
| 115                   | 249                      | 2108789  | BRAITUT03 | 2108789H1 and 2108789R6 (BRAITUT03), 2182008T6 (SININOT01), 3255751R6 and 3255751T6 (OVRTUT01)   |
| 116                   | 250                      | 2171401  | ENDCN0T03 | 037241F1 (HUVENOB01), 1821492F6 (GBLATUT01), 2055814T6 (BEPINOT01), 2171401F6 and 2171401H1 (ENDCN0T03), 2668952F6 (ESOGTUT02), 3140313H1 and 3140313T6 (SMCCN0T02), 5031775H1 (EPIBTXT01)   |
| 117                   | 251                      | 2212530  | SINTFET03 | 187596R6 and 187596T6 (CARDNOT01), 919634R6 (RATRN0T02), 1992331H1 (CORPNOT02), 2062034H1 (OVARNOT03), 2212530F6 and 2212530H1 (SINTFET03), 2520479H1 (BRAITUT21), 2878284F6 (THYRN0T10), 2992354H1 (KIDNFET02), 4020719F6 (BRAXN0T02) |
| 118                   | 252                      | 2253036  | OVRTUT01  | 2253036H1 and 2253036R6 (OVRTUT01)   |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments  |
|-----------------------|--------------------------|----------|-----------|--|
| 119                   | 253                      | 2280161  | PROSNON01 | 482326H1 (HNT2RAT01), 934345H1 (CERVNOT01), 1379358F1 and 1379358T1 (LUNGNOT10), 1438562T1 (PANCNOT08), 1467511F6 (PANCNOT02), 1568138F1 (UTRSNOT05), 1636106T6 (UTRSNOT06), 2134534F6 (ENDCNOT01), 2280161H1 and 2280161X19F1 (PROSNON01), 2789845F6 (COLNTUT16), 3096938H1 (CERVNOT03), 3774621F6 (BRSTNOT25), 4222971H1 (PANCNOT07), 5111983H1 (ENDITXT01), 5324177H1 (FIBPFEN06) |
| 120                   | 254                      | 2287485  | BRAINON01 | 1454588F1 (PENITUT01), 1593332F6 (BRAINOT14), 2287485H1 and 2287485R6 (BRAINON01), 3765992H1 (BRSTNOT24), 4374293H1 (CONFNOT03), 4937931H1 (PROSTUS18), SBCA01722F1  |
| 121                   | 255                      | 2380344  | ISLTNOT01 | 2380344F6 and 2380344H1 (ISLTNOT01), 2888536T3 (LUNGFET04), SASA03644F1, SASA03689F1   |
| 122                   | 256                      | 2383171  | ISLTNOT01 | 956296R1 (KIDNNOT05), 1342250F1 (COLNTUT03), 1468046F1 and 1468046T1 (PANCNOT02), 2383171H1 (ISLTNOT01), SBYA05452U1, SBYA01369U1  |
| 123                   | 257                      | 2396046  | THPIAZT01 | 2396046F6, 2396046H1 and 2396118T6 (THPIAZT01)   |
| 124                   | 258                      | 2456587  | ENDANOT01 | 2456587H1 and 2456587T6 (ENDANOT01), 2872569H1 (THYRNOT10), SBCA03778F1, SBDA00115F1, SBCA02401F1, SBCA03351F1, SBCA05164F1, SBCA04783F1, SBCA00155F1, SBCA04141F1   |
| 125                   | 259                      | 2484813  | BONRTUT01 | 1234970T1 (LUNGFET03), 1338090F6 (COLNNOT13), 2484813H1 (BONRTUT01), SBCA00053F1, SBCA02064F1, SBCA02151F1, SBCA03770F1, SBCA04866F1, SBCA03406F1  |
| 126                   | 260                      | 2493851  | ADRETUT05 | 2493851H1 (ADRETUT05), 3805916F6 (BLADTUT03), 4500439H1 and 4500748H1 (BRAVXT02), 5120601H1 (SMCBUNT01)  |
| 127                   | 261                      | 2495719  | ADRETUT05 | 603447R1 (BRSTTUT01), 2495719H1 (ADRETUT05), 2917493F6 (THYMFET03), 4647103H1 (PROSTUT20), SBRA04984D1   |

TABLE 1 (cont.)

| Protein<br>SEQ ID NO: | Nucleotide<br>SEQ ID NO: | Clone ID | Library   | Fragments   |
|-----------------------|--------------------------|----------|-----------|---|
| 128                   | 262                      | 2614153  | GBLANOT01 | 1833135R6 (BRAINON01), 1966515R6 (BRSTNOT04), 2331103R6 (COLNNOT11), 2614153H1 (GBLANOT01), 2656691F6 (LUNGUTUT09), 3951176H1 (DRGCNOT01) |
| 129                   | 263                      | 2655184  | THYMNOT04 | 2655184H1 (THYMNOT04), SBDA05215F1, SBDA05213F1, SBDA01516F1  |
| 130                   | 264                      | 2848362  | BRSTTUT13 | 1297974F1 and 1297974T6 (BRSTNOT07), 2630138F6 (COLNTUT15), 2848362H1 (BRSTTUT13)   |
| 131                   | 265                      | 2849906  | BRSTTUT13 | 1541617R1 and 1541617T1 (SINTTUT01), 2684504F6 and 2684504T6 (LUNGNOT23), 2796805H1 (NPOLNOT01), 2849906H1 (BRSTTUT13)                    |
| 132                   | 266                      | 2899137  | DRGCNOT01 | 2899137H1 (DRGCNOT01), 3026490F6 and 3026490T6 (HEARFET02), 3483359H1 (KIDNNOT31)   |
| 133                   | 267                      | 2986229  | CARGDIT01 | 1740227T6 (HIPONON01), 2986229H1 (CARGDIT01)  |
| 134                   | 268                      | 3222081  | COLNNON03 | 1754079F6 (LIVRTUT01), 3222081H1 (COLNNON03), 4053813T6 (SPLNNOT13), 4230282H1 (BRAMDIT01), SBDA07029F3                                   |

TABLE 2

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites          | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification | Analytical<br>Methods |
|-----------------------|---------------------------|---|-------------------------------------|---------------------|----------------|-----------------------|
| 1                     | 88                        | T83 S38 T76                                 |                                     | M1 - A21            |                | Signal Peptide<br>HMM |
| 2                     | 128                       | S30 S40 T47 T119<br>W125                    |                                     | M1 - F28            |                | Signal Peptide<br>HMM |
| 3                     | 111                       | T70   |                                     | M1 - T18            |                | Signal Peptide<br>HMM |
| 4                     | 110                       | S32 T64                                     | N58                                 | M1 - A29            |                | Signal Peptide<br>HMM |
| 5                     | 78                        | T27 S39 S39 S44 S22<br>T27 S28 S57          |                                     | M1 - R24            |                | Signal Peptide<br>HMM |
| 6                     | 88                        | T55 S30 S40 T55                             | N34                                 | M1 - N21            |                | Signal Peptide<br>HMM |
| 7                     | 227                       | S220 S70 S83 T131<br>S134 S141 T158<br>Y123 | N100                                | M1 - Q20            |                | Signal Peptide<br>HMM |
| 8                     | 198                       | S62 T123 S142 S189<br>S62 T100 Y85          | N60                                 | M1 - A28            |                | Signal Peptide<br>HMM |
| 9                     | 65                        | T48   |                                     | M1 - A29            |                | Signal Peptide<br>HMM |
| 10                    | 154                       |   |                                     | M1 - A29            |                | Signal Peptide<br>HMM |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites                               | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification | Analytical<br>Methods |
|-----------------------|---------------------------|--|-------------------------------------|---------------------|----------------|-----------------------|
| 11                    | 237                       | T116 T26 T79 T85<br>T182 T188 T194<br>T206 S60 S123 S176<br>S213 | N128                                | M1 - A19            |                | Signal Peptide<br>HMM |
| 12                    | 225                       | T158 S128  | N166                                | M1 - G27            |                | Signal Peptide<br>HMM |
| 13                    | 117                       | S41  |                                     | M1 - A23            |                | Signal Peptide<br>HMM |
| 14                    | 253                       | S49 T63 S92 T110<br>S127 T239                                    | N42 N47 N72<br>N207                 | M1 - T20            |                | Signal Peptide<br>HMM |
| 15                    | 171                       | S43 S94 T114   |                                     | M88 - R112          |                | Signal Peptide<br>HMM |
| 16                    | 78                        | S38 S43  | N37                                 | M1 - G19            |                | Signal Peptide<br>HMM |
| 17                    | 71                        | T64 T67  |                                     | M1 - C19            |                | Signal Peptide<br>HMM |
| 18                    | 188                       | S36 T58 T133 Y31   | N121 N171                           | M1 - A21            |                | Signal Peptide<br>HMM |
| 19                    | 80                        | S76  |                                     | M1 - C19            |                | Signal Peptide<br>HMM |
| 20                    | 80                        |  |                                     | M1 - G25            |                | Signal Peptide<br>HMM |
| 21                    | 84                        | S39 S53 S60  |                                     | M1 - G21            |                | Signal Peptide<br>HMM |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites   | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification | Analytical<br>Methods |
|-----------------------|---------------------------|--|-------------------------------------|---------------------|----------------|-----------------------|
| 22                    | 171                       | S41 T150   |                                     | M3 - A21            |                | Signal Peptide<br>HMM |
| 23                    | 243                       | S3 S44 T75 S86 S183<br>S223 S36 S92 S205<br>Y40 Y110                                   | N97                                 | M1 - C25            |                | Signal Peptide<br>HMM |
| 24                    | 311                       | T5 S76 T82 T93<br>T109 S121 T137<br>T170 S184 S11 T53<br>S75 S84 T132 S223<br>S274 Y69 | N49 N91 N108<br>N128 N135<br>N190   | M1 - A32            |                | Signal Peptide<br>HMM |
| 25                    | 57                        |  |                                     | M1 - L29            |                | Signal Peptide<br>HMM |
| 26                    | 82                        | S46 Y26  |                                     | M1 - S18            |                | Signal Peptide<br>HMM |
| 27                    | 115                       |  |                                     | M1 - G34            |                | Signal Peptide<br>HMM |
| 28                    | 327                       | S93 S50 S167 S233<br>S89 T105 T214 S302<br>T318  | N138 N206                           | M1 - E25            |                | Signal Peptide<br>HMM |
| 29                    | 133                       | S63  | N105                                | M1 - E29            |                | Signal Peptide<br>HMM |
| 30                    | 129                       | S21 S65 T93  |                                     | M1 - G20            |                | Signal Peptide<br>HMM |

TABLE 2

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites          | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification | Analytical<br>Methods |
|-----------------------|---------------------------|---|-------------------------------------|---------------------|----------------|-----------------------|
| 1                     | 88                        | T83 S38 T76                                 |                                     | M1 - A21            |                | Signal Peptide<br>HMM |
| 2                     | 128                       | S30 S40 T47 T119<br>W125                    |                                     | M1 - F28            |                | Signal Peptide<br>HMM |
| 3                     | 111                       | T70   |                                     | M1 - T18            |                | Signal Peptide<br>HMM |
| 4                     | 110                       | S32 T64                                     | N58                                 | M1 - A29            |                | Signal Peptide<br>HMM |
| 5                     | 78                        | T27 S39 S39 S44 S22<br>T27 S28 S57          |                                     | M1 - R24            |                | Signal Peptide<br>HMM |
| 6                     | 88                        | T55 S30 S40 T55                             | N34                                 | M1 - N21            |                | Signal Peptide<br>HMM |
| 7                     | 227                       | S220 S70 S83 T131<br>S134 S141 T158<br>Y123 | N100                                | M1 - Q20            |                | Signal Peptide<br>HMM |
| 8                     | 198                       | S62 T123 S142 S189<br>S62 T100 Y85          | N60                                 | M1 - A28            |                | Signal Peptide<br>HMM |
| 9                     | 65                        | T48   |                                     | M1 - A29            |                | Signal Peptide<br>HMM |
| 10                    | 154                       |   |                                     | M1 - A29            |                | Signal Peptide<br>HMM |



TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites                               | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification | Analytical<br>Methods |
|-----------------------|---------------------------|--|-------------------------------------|---------------------|----------------|-----------------------|
| 11                    | 237                       | T116 T26 T79 T85<br>T182 T188 T194<br>T206 S60 S123 S176<br>S213 | N128                                | M1 - A19            |                | Signal Peptide<br>HMM |
| 12                    | 225                       | T158 S128  | N166                                | M1 - G27            |                | Signal Peptide<br>HMM |
| 13                    | 117                       | S41  |                                     | M1 - A23            |                | Signal Peptide<br>HMM |
| 14                    | 253                       | S49 T63 S92 T110<br>S127 T239                                    | N42 N47 N72<br>N207                 | M1 - T20            |                | Signal Peptide<br>HMM |
| 15                    | 171                       | S43 S94 T114   |                                     | M88 - R112          |                | Signal Peptide<br>HMM |
| 16                    | 78                        | S38 S43  | N37                                 | M1 - G19            |                | Signal Peptide<br>HMM |
| 17                    | 71                        | T64 T67  |                                     | M1 - C19            |                | Signal Peptide<br>HMM |
| 18                    | 188                       | S36 T58 T133 Y31   | N121 N171                           | M1 - A21            |                | Signal Peptide<br>HMM |
| 19                    | 80                        | S76  |                                     | M1 - C19            |                | Signal Peptide<br>HMM |
| 20                    | 80                        |  |                                     | M1 - G25            |                | Signal Peptide<br>HMM |
| 21                    | 84                        | S39 S53 S60  |                                     | M1 - G21            |                | Signal Peptide<br>HMM |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites   | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification | Analytical<br>Methods |
|-----------------------|---------------------------|--|-------------------------------------|---------------------|----------------|-----------------------|
| 22                    | 171                       | S41 T150   |                                     | M3 - A21            |                | Signal Peptide<br>HMM |
| 23                    | 243                       | S3 S44 T75 S86 S183<br>S223 S36 S92 S205<br>Y40 Y110                                   | N97                                 | M1 - C25            |                | Signal Peptide<br>HMM |
| 24                    | 311                       | T5 S76 T82 T93<br>T109 S121 T137<br>T170 S184 S11 T53<br>S75 S84 T132 S223<br>S274 Y69 | N49 N91 N108<br>N128 N135<br>N190   | M1 - A32            |                | Signal Peptide<br>HMM |
| 25                    | 57                        |  |                                     | M1 - L29            |                | Signal Peptide<br>HMM |
| 26                    | 82                        | S46 Y26  |                                     | M1 - S18            |                | Signal Peptide<br>HMM |
| 27                    | 115                       |  |                                     | M1 - G34            |                | Signal Peptide<br>HMM |
| 28                    | 327                       | S93 S50 S167 S233<br>S89 T105 T214 S302<br>T318  | N138 N206                           | M1 - E25            |                | Signal Peptide<br>HMM |
| 29                    | 133                       | S63  | N105                                | M1 - E29            |                | Signal Peptide<br>HMM |
| 30                    | 129                       | S21 S65 T93  |                                     | M1 - G20            |                | Signal Peptide<br>HMM |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites  | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification                               | Analytical<br>Methods                       |
|-----------------------|---------------------------|---|-------------------------------------|---------------------|--|---|
| 31                    | 472                       | S164 T32 S42 T141<br>T154 S155 T235<br>T262 T271 T334<br>T376 S402 S421<br>S435 T441 S19 S29<br>T327 S378 | N61 N179 N353<br>N356 N396          | M1 - G20            | hematopoietic lineage switch 2<br>(g3169729) | Signal Peptide<br>HMM<br>BLAST -<br>GenBank |
| 32                    | 93                        | T21   |                                     | M1 - A18            |  | Signal Peptide<br>HMM                       |
| 33                    | 92                        | S57 S5  |                                     | M1 - G47            |  | SPScan                                      |
| 34                    | 143                       | T6 T14 T135   |                                     | M9 - G40            |  | Signal Peptide<br>HMM                       |
| 35                    | 89                        | T15 S58 S66   |                                     | M1 - A19            |  | Signal Peptide<br>HMM                       |
| 36                    | 560                       | T7 T76 S150 T224<br>S228 S257 S358<br>S474 S529 S539<br>T186 S219 S368<br>Y523                            | N163 N184<br>N379                   | M1 - E34            |  | SPScan                                      |
| 37                    | 197                       | T80 S163  |                                     | M1 - G28            |  | Signal Peptide<br>HMM                       |
| 38                    | 437                       | T47 T146 S233 S391<br>S403 T43 S130 S273<br>S339 S364   | N46 N189 N382                       | M1 - A21            |  | Signal Peptide<br>HMM                       |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites                               | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification  | Analytical<br>Methods                       |
|-----------------------|---------------------------|--|-------------------------------------|---------------------|---|---|
| 39                    | 330                       | S197 T49 T150 S193<br>T214 T215 T49 S111<br>S237                 | N46 N64 N166<br>N191                | M1 - G28            |   | Signal Peptide<br>HMM                       |
| 40                    | 148                       | T73 S141   | N29 N58 N71<br>N103                 | M1 - R24            | receptor-activity-modifying protein<br>(RAMP; g4163368) | Signal Peptide<br>HMM<br>BLAST -<br>GenBank |
| 41                    | 188                       | S49  |                                     | M1 - V25            |   | Signal Peptide<br>HMM                       |
| 42                    | 222                       | S89 S165 T174 T182<br>T83 S155                                   |                                     | M1 - S24            |   | Signal Peptide<br>HMM                       |
| 43                    | 111                       | S54 S29 S98 S50 S57<br>T104                                      |                                     | M1 - T23            |   | Signal Peptide<br>HMM                       |
| 44                    | 341                       | T29 S106 T120 S161<br>S195 S37 S47 T51<br>S136 S223 S230<br>S281 |                                     | M1 - G22            |   | Signal Peptide<br>HMM                       |
| 45                    | 148                       | S21 T63 T63 A146   | N40                                 | M1 - G23            |   | Signal Peptide<br>HMM                       |
| 46                    | 87                        | S65  |                                     | M1 - P18            |   | Signal Peptide<br>HMM                       |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites                        | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification  | Analytical<br>Methods                       |
|-----------------------|---------------------------|---|-------------------------------------|---------------------|---|---|
| 47                    | 383                       | T77 S95 S108 S280<br>S351 S121 S124<br>S153 T187          | N93 N207                            | M1 - P23            |   | Signal Peptide<br>HMM                       |
| 48                    | 109                       | S25 S22   |                                     | M1 - L18            |   | Signal Peptide<br>HMM                       |
| 49                    | 185                       | S62   |                                     | M1 - A20            |   | Signal Peptide<br>HMM                       |
| 50                    | 110                       | T100 T73 S97 Y48  | N71                                 | M1 - C21            |   | Signal Peptide<br>HMM                       |
| 51                    | 126                       | S17 S110  |                                     | M1 - G18            |   | Signal Peptide<br>HMM                       |
| 52                    | 488                       | S205 T31 S86 T236<br>S7 T447                              | N250 N321<br>N463                   | M1 - L25            | putative involvement in cell wall<br>structure or biosynthesis (g3738170) | Signal Peptide<br>HMM<br>BLAST -<br>GenBank |
| 53                    | 197                       | T55 S34 S46 S69 T98<br>S108 T119 T167<br>S194 S2 S34 T153 |                                     | M1 - A26            |   | Signal Peptide<br>HMM                       |
| 54                    | 84                        | S65 S36 T41 S51 S69<br>S81                                | N39                                 | M1 - G25            |   | Signal Peptide<br>HMM                       |
| 55                    | 97                        | S56   |                                     | M1 - A22            |   | Signal Peptide<br>HMM                       |
| 56                    | 140                       | S29   |                                     | M1 - P23            |   | Signal Peptide<br>HMM                       |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites                           | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification              | Analytical<br>Methods                       |
|-----------------------|---------------------------|--|-------------------------------------|---------------------|-----------------------------|---|
| 57                    | 285                       | S53 S108 T216 S253<br>S277                                   | N153                                | M1 - A25            |                             | Signal Peptide<br>HMM                       |
| 58                    | 262                       | S62 T166 S62 S71<br>Y246                                     | N190                                | M1 - G28            | 3-acylating enzyme (Q44449) | Signal Peptide<br>HMM<br>BLAST -<br>GENESEQ |
| 59                    | 189                       | S120 T154 T34 T37<br>S174                                    |                                     | M1 - C22            |                             | Signal Peptide<br>HMM                       |
| 60                    | 257                       | S98 T136 T67 S112<br>S234 S237                               |                                     | M55 - E84ß          |                             | SPScan                                      |
| 61                    | 82                        | T68  | N67                                 | M1 - G18            |                             | Signal Peptide<br>HMM                       |
| 62                    | 202                       | T21 S117 S120  |                                     | M1 - G27            |                             | Signal Peptide<br>HMM                       |
| 63                    | 450                       | S107 S97 S146 S339<br>S440 S245 T303<br>S304 S399            |                                     | M1 - G18            |                             | Signal Peptide<br>HMM                       |
| 64                    | 322                       | T145 T214 T16 S24<br>S35 S45 T145 T269<br>S297 T300 T314 Y87 | N53 N130 N289                       | M1 - G23            |                             | Signal Peptide<br>HMM                       |
| 65                    | 104                       | S38 S25 S75  |                                     | M1 - A18            |                             | Signal Peptide<br>HMM                       |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites                     | Potential<br>Glycosylation<br>Sites | Signature Sequences   | Identification | Analytical<br>Methods   |
|-----------------------|---------------------------|--|-------------------------------------|---|----------------|-------------------------|
| 66                    | 93                        |  |                                     | M1 through about S18<br>Transmembrane:<br>M1 through about Y17  |                | SPscan<br>HMM           |
| 67                    | 71                        | S23 S64  |                                     | M1 through about A24  |                | SPscan<br>HMM<br>MOTIFS |
| 68                    | 394                       | S392 S393 S31 S127<br>S179 S334 T338<br>S358 T383 Y323 | N53                                 | M1 through about S31<br>Transmembrane:<br>about M159 through about F178<br>about F109 through about S127<br>about F225 through about V243 |                | SPScan<br>HMM<br>MOTIFS |
| 69                    | 72                        | S59  | N69                                 | M1 through about S23<br>Transmembrane:<br>M1 through about L16  |                | SPscan<br>HMM<br>MOTIFS |
| 70                    | 71                        | S11 T26  |                                     | M1 through about Q18  |                | SPscan<br>HMM<br>MOTIFS |
| 71                    | 247                       | S41 T79  |                                     | M1 through about S25  |                | SPscan<br>HMM<br>MOTIFS |
| 72                    | 73                        | S56  |                                     | M1 through about G27  |                | SPscan<br>HMM<br>MOTIFS |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites | Potential<br>Glycosylation<br>Sites | Signature Sequences   | Identification | Analytical<br>Methods   |
|-----------------------|---------------------------|------------------------------------|-------------------------------------|---|----------------|-------------------------|
| 73                    | 70                        |                                    |                                     | M1 through about G20  |                | SPscan<br>HMM           |
| 74                    | 67                        |                                    |                                     | M1 through about G30  |                | SPscan<br>HMM           |
| 75                    | 91                        |                                    |                                     | M1 through about G26  |                | SPScan                  |
| 76                    | 56                        | T29 S46 T51                        |                                     | M1 through about S19  |                | SPscan<br>HMM<br>MOTIFS |
| 77                    | 112                       | S62 S65                            |                                     | M1 through about G27<br>Transmembrane:<br>about W79 through about H97 |                | SPscan<br>HMM<br>MOTIFS |
| 78                    | 54                        |                                    | N48                                 | M1 through about N34  |                | SPscan<br>HMM<br>MOTIFS |
| 79                    | 57                        | T33 R55                            |                                     | M1 through about C18  |                | SPscan<br>HMM<br>MOTIFS |
| 80                    | 52                        | S34                                |                                     | M1 through about S30  |                | SPscan<br>HMM<br>MOTIFS |



TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites | Potential<br>Glycosylation<br>Sites | Signature Sequences  | Identification | Analytical<br>Methods   |
|-----------------------|---------------------------|------------------------------------|-------------------------------------|--|----------------|-------------------------|
| 81                    | 64                        | T43 Y27                            |                                     | M1 through about S41   |                | SPscan<br>HMM<br>MOTIFS |
| 82                    | 65                        | S45                                |                                     | M1 through about A31<br>Transmembrane:<br>about L38 through about F55        |                | SPscan<br>HMM<br>MOTIFS |
| 83                    | 56                        |                                    |                                     | M1 through about E23   |                | SPscan<br>HMM           |
| 84                    | 120                       | S69 S109                           | N89 N95                             | M1 through about A38<br>Transmembrane: about L23<br>through about T41        |                | SPscan<br>HMM<br>MOTIFS |
| 85                    | 67                        | S28                                |                                     | M1 through about K30<br>Microbodies C-terminal<br>targeting signal:<br>A65KV |                | SPscan<br>HMM<br>MOTIFS |
| 86                    | 62                        | S29 S42 S46                        | N40                                 | M1 through about S29   |                | SPscan<br>HMM<br>MOTIFS |
| 87                    | 75                        | S25 S46                            |                                     | M1 through about L19<br>Transmembrane:<br>about I3 through about G20         |                | SPscan<br>HMM<br>MOTIFS |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites   | Potential<br>Glycosylation<br>Sites | Signature Sequences   | Identification | Analytical<br>Methods                |
|-----------------------|---------------------------|--|-------------------------------------|---|----------------|--------------------------------------|
| 88                    | 80                        | T28  |                                     | M1 through about A20  |                | SPscan<br>HMM<br>MOTIFS              |
| 89                    | 50                        | S11  |                                     | M1 through about C48  |                | SPscan<br>HMM<br>MOTIFS              |
| 90                    | 116                       | S38  |                                     | M1 through about G22  |                | SPscan<br>HMM<br>MOTIFS              |
| 91                    | 67                        | S43  |                                     | M1 through about P21  |                | SPscan<br>HMM<br>MOTIFS              |
| 92                    | 538                       | S415 S52 T77 S97<br>T178 T228 S282<br>S320 S337 S384<br>T401 T424 S483<br>S207 S230 S357<br>T410 Y263 Y365 | N226                                | M1 through about S18<br>Tyrosine specific protein<br>phosphatases signature:<br>about V328 through about F340 |                | SPScan<br>BLOCKS<br>PRINTS<br>MOTIFS |
| 93                    | 58                        |  |                                     | M1 through about S25  |                | SPscan<br>HMM                        |
| 94                    | 119                       | S39  |                                     | M1 through about S22<br>Transmembrane:<br>about V3 through about S21  |                | SPscan<br>HMM<br>MOTIFS              |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites    | Potential<br>Glycosylation<br>Sites            | Signature Sequences  | Identification | Analytical<br>Methods                      |
|-----------------------|---------------------------|---------------------------------------|--|--|----------------|--|
| 95                    | 128                       | S91                                   |  | M1 through about G31<br>Transmembrane:<br>about F108 through about L126                  |                | SPScan<br>HMM<br>MOTIFS                    |
| 96                    | 124                       | T115 T43 S91                          |  | M1-S20<br>P116-V124<br>(urotensin II<br>signature)                                       |                | SPScan<br>HMM<br>Motifs<br>BLOCKS<br>BLAST |
| 97                    | 182                       | S28 T70 S172 S25<br>S32 S48 S108 S131 |  | M1-S23, M1-S25   |                | SPScan<br>HMM<br>Motifs                    |
| 98                    | 237                       | S55 S88 S121 S135                     | N45 N73 N107<br>N118 N132<br>N172 N175<br>N185 | M1-A16, M1-S21<br>C40-C198<br>(cysteine spacing<br>pattern similar<br>to that of RoBo-I) |                | SPScan<br>HMM<br>Motifs<br>BLAST           |
| 99                    | 160                       | S36 S59 T143                          |  | M1-A27   |                | SPScan<br>HMM<br>Motifs                    |
| 100                   | 148                       | T76 S64 Y103                          |  | M1-S30, M1-G31   |                | SPScan<br>HMM<br>Motifs                    |
| 101                   | 170                       | S78 T4 T30 S130 S25<br>S29 T122       |  | M1-A23, M1-L28   |                | SPScan<br>HMM<br>Motifs                    |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites | Potential<br>Glycosylation<br>Sites | Signature Sequences | Identification | Analytical<br>Methods   |
|-----------------------|---------------------------|------------------------------------|-------------------------------------|---------------------|----------------|-------------------------|
| 102                   | 150                       | S50 S78 S91                        |                                     | M1-A26, M1-S28      |                | SPScan<br>HMM<br>Motifs |
| 103                   | 142                       | T57 T80                            |                                     | M1-A25, M1-G26      |                | SPScan<br>HMM<br>Motifs |
| 104                   | 110                       | T3                                 |                                     | M1-G18, M1-T25      |                | SPScan<br>HMM<br>Motifs |
| 105                   | 120                       | T29 S40 S72                        |                                     | M1-G22, M1-A20      |                | SPScan<br>HMM<br>Motifs |
| 106                   | 135                       | T115 S38 T41                       | N32 N101                            | M1-G26, M1-C25      |                | SPScan<br>HMM<br>Motifs |
| 107                   | 301                       | S53 S217 S240 S283<br>T224         |                                     | M1-A22              |                | SPScan<br>HMM<br>Motifs |
| 108                   | 103                       | S88 T73 S84                        |                                     | M1-P19, M1-L22      |                | SPScan<br>HMM<br>Motifs |
| 109                   | 95                        | T82 S52 S77                        | N50                                 | M1-T15, M1-P19      |                | SPScan<br>HMM<br>Motifs |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites   | Potential<br>Glycosylation<br>Sites | Signature Sequences   | Identification   | Analytical<br>Methods                         |
|-----------------------|---------------------------|--|-------------------------------------|-----------------------|--|---|
| 110                   | 113                       | T84 S4   |                                     | M1-P19, M1-A24        |  | SPScan<br>HMM<br>Motifs                       |
| 111                   | 234                       | S179 S184 S51 T70<br>T158 S168 T228 Y29  | N146 N191<br>N194                   | M1-A20                | NK cell activating receptor<br>(g4493702)                    | SPScan<br>HMM<br>Motifs<br>BLAST -<br>GenBank |
| 112                   | 119                       | S39 T61  |                                     | M1-G30, M1-G27        |  | SPScan<br>HMM<br>Motifs                       |
| 113                   | 200                       | S51 T46 S191   |                                     | M1-G26 Signal Peptide | Signal Peptide Containing Protein,<br>Homology with KIAA0206 | SPScan<br>Motifs<br>BLAST                     |
| 114                   | 225                       |  |                                     | M1-Q29 Signal Peptide | Signal Peptide Containing Protein                            | SPScan  |
| 115                   | 155                       | S29  |                                     | M1-A20 Signal Peptide | Signal Peptide Containing Protein                            | HMM<br>Motifs                                 |
| 116                   | 468                       | S143 T156 T227<br>S235 T271 T293<br>T436 S453 S117<br>T148 T213 S263<br>S417 Y73 | N280 N384                           | M1-G23 Signal Peptide | Signal Peptide Containing Protein                            | SPScan<br>Motifs                              |
| 117                   | 403                       | S19 S320 S69 S151<br>T171 T97 S393 Y193<br>Y378                                  | N87                                 | M1-A24 Signal Peptide | Signal Peptide Containing Protein                            | HMM<br>Motifs                                 |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites  | Potential<br>Glycosylation<br>Sites | Signature Sequences  | Identification  | Analytical<br>Methods            |
|-----------------------|---------------------------|---|-------------------------------------|--|---|----------------------------------|
| 118                   | 131                       | T131 S24 T79 T118<br>T123 T127  | N116                                | M1-G25 Signal Peptide  | Signal Peptide Containing Protein   | SPScan<br>Motifs                 |
| 119                   | 556                       | T176 S192 S196<br>T220 S344 S369<br>S476 T501 S529<br>S541 T548 T553 S48<br>S115 S121 T386<br>T424 S500<br>Y104 | N62 N79 N127<br>N157 N160           | M1-P21 Signal Peptide<br>L226-W244, Y402-W422,<br>V375-L392 and Y355-I376<br>Transmembrane Domains | Signal Peptide Containing Protein,<br>Weakly similar to Putative<br>Transmembrane Protein (PTM1)<br>Precursor | SPScan<br>Motifs<br>HMM<br>BLAST |
| 120                   | 514                       | T457 T80 S86 T141<br>T372 T420 S447 S94<br>T102 S112 T240<br>S297 S353 S470                                     | N100 N168<br>N319                   | M1-G24 Signal Peptide  | Signal Peptide Containing Protein,  | SPScan<br>Motifs                 |
| 121                   | 109                       | T46 S78 T12   |                                     | M1-S15 Signal Peptide  | Signal Peptide Containing Protein   | SPScan<br>Motifs                 |
| 122                   | 431                       | S57 T320 S339 S396<br>S100 S239   |                                     | M1-L25 Signal Peptide  | Signal Peptide Containing Protein,<br>Weakly similar to OXA1L   | SPScan<br>Motifs<br>BLAST        |
| 123                   | 142                       |   |                                     | M1-W16 Signal Peptide  | Signal Peptide Containing Protein   | SPScan                           |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites  | Potential<br>Glycosylation<br>Sites | Signature Sequences   | Identification  | Analytical<br>Methods                                 |
|-----------------------|---------------------------|---|-------------------------------------|---|---|---|
| 124                   | 643                       | T8 S28 S77 T169<br>T199 T235 S252<br>T320 S402 T413<br>S414 S558 S22 T25<br>S56 S62 S120 T184<br>S329 T423 S475<br>S574 Y226        | N251                                | M1-S28 Signal Peptide,<br>D37-C81, W380-C437, W440-<br>C492 and F526-C583<br>Thrombospondin Type 1<br>Domains | Signal Peptide Containing Protein,<br>Thrombospondin Type 1 Protein     | SPScan<br>Motifs<br>Pfam<br>BLAST                     |
| 125                   | 568                       | S510 T24 T80 S91<br>T153 T165 S232<br>S248 S262 T300<br>T334 S380 S446 S16<br>T19 T60 S127 S273<br>T436 T531 S554<br>T564 Y135 Y489 | N322                                | M1-T19 Signal Peptide   | Signal Peptide Containing Protein                                       | SPScan<br>Motifs                                      |
| 126                   | 125                       | T62 S27 T36   |                                     | M1-R32 Signal Peptide,<br>V4-L53 Glycosyl Hydrolase<br>Family 9 Active Site Signature                         | Signal Peptide Containing Protein,<br>Glycosyl Hydrolase Protein        | SPScan<br>Motifs<br>PROFILE-<br>SCAN                  |
| 127                   | 196                       | T105 T47 T56 S158   |                                     | M1-S26 Signal Peptide,<br>H79-H123 Ribosomal Protein<br>S18 Signature   | Signal Peptide Containing Protein,<br>Ribosomal Protein S18             | SPScan<br>Motifs<br>BLAST<br>Pfam<br>PROFILE-<br>SCAN |
| 128                   | 214                       | S112 S131   | N37 N92                             | M1-S35 Signal Peptide   | Signal Peptide Containing Protein,<br>Homology with GTP Binding Protein | SPScan<br>Motifs<br>BLAST                             |

TABLE 2 (cont.)

| Protein<br>SEQ ID NO: | Amino<br>Acid<br>Residues | Potential<br>Phosphorylation Sites   | Potential<br>Glycosylation<br>Sites | Signature Sequences   | Identification  | Analytical<br>Methods                     |
|-----------------------|---------------------------|--------------------------------------|-------------------------------------|---|---|---|
| 129                   | 88                        |                                      |                                     | M1-S24 Signal Peptide   | Signal Peptide Containing Protein   | HMM                                       |
| 130                   | 260                       | S146 S179 S192<br>S239 S70 T126 T150 | N50 N109                            | M1-A48 Signal Peptide,<br>G59-S142 Immunoglobulin<br>Domain   | Signal Peptide Containing Protein,<br>Immunoglobulin Superfamily Protein  | SPScan<br>Motifs<br>Pfam                  |
| 131                   | 295                       | T176 T56 S72 S179<br>S256 S87        |                                     | M1-A30 Signal Peptide   | Signal Peptide Containing Protein   | SPScan<br>Motifs                          |
| 132                   | 183                       | S11 T41 T42 S83                      |                                     | M1-W24 Signal Peptide,<br>E131-K168 and C105-H115<br>Adrenodoxin Iron-Sulfur<br>Binding Signature,<br>C111-V116 Cytochrome C<br>Heme Binding Signature,<br>N69-A162 Iron-Sulfur Cluster<br>Binding Domain | Signal Peptide Containing Protein,<br>Adrenodoxin Family Iron-Sulfur<br>Binding Protein, and<br>Cytochrome C Family Heme Binding<br>Protein | HMM<br>Motifs<br>BLOCKS<br>PRINTS<br>Pfam |
| 133                   | 113                       | S93 T89 Y9                           |                                     | M1-G30 Signal Peptide,<br>V28-L74 PF00646 F-Box<br>Domain   | Signal Peptide Containing Protein,<br>PF00646 F-Box Protein   | SPScan<br>Motifs<br>Pfam                  |
| 134                   | 160                       | T46 T55 S65 S124<br>T125 T46         |                                     | M1-A27 Signal Peptide   | Signal Peptide Containing Protein,<br>F45G2.10 and Yhr122wp Homology  | SPScan<br>Motifs<br>BLAST                 |



TABLE 3

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction) | Vector      |
|--------------------------|---|--|-------------|
| 135                      | Hematopoietic/Immune (1.000)  | Inflammation (1.000)   | pBLUESCRIPT |
| 136                      | Hematopoietic/Immune (0.750) Cardiovascular (0.250)                           | Inflammation (0.750) Cancer (0.250)                          | pSPORT1     |
| 137                      | Nervous (1.000)   | Trauma (1.000)   | pSPORT1     |
| 138                      | Musculoskeletal (1.000)   | Inflammation (1.000)   | pSPORT1     |
| 139                      | Gastrointestinal (0.714) Cardiovascular (0.143)<br>Reproductive (0.143)       | Cancer (0.714) Trauma (0.143)                                | pSPORT1     |
| 140                      | Nervous (1.000)   | Neurological (0.500) Trauma (0.500)                          | pSPORT1     |
| 141                      | Reproductive (0.293) Gastrointestinal (0.146)<br>Hematopoietic/Immune (0.146) | Cancer (0.524) Inflammation (0.256) Fetal (0.146)            | pSPORT1     |
| 142                      | Reproductive (0.266) Gastrointestinal (0.170)<br>Nervous (0.138)              | Cancer (0.479) Inflammation (0.277) Fetal (0.181)            | pINCY       |
| 143                      | Reproductive (0.417) Nervous (0.292)<br>Developmental (0.125)                 | Cancer (0.417) Inflammation (0.250) Fetal (0.167)            | pINCY       |
| 144                      | Reproductive (0.321) Cardiovascular (0.143)<br>Developmental (0.143)          | Cancer (0.464) Fetal (0.214) Inflammation (0.143)            | pINCY       |
| 145                      | Reproductive (0.600) Gastrointestinal (0.400)                                 | Cancer (0.400) Trauma (0.400) Inflammation (0.200)           | pINCY       |
| 146                      | Cardiovascular (0.400) Dermatologic (0.200)<br>Nervous (0.200)                | Cancer (0.600) Fetal (0.600)                                 | pINCY       |
| 147                      | Developmental (0.667) Gastrointestinal (0.333)                                | Fetal (0.667) Cancer (0.333)                                 | pINCY       |
| 148                      | Reproductive (0.256) Nervous (0.248)<br>Cardiovascular (0.137)                | Cancer (0.479) Inflammation (0.214) Fetal (0.145)            | pINCY       |
| 149                      | Reproductive (0.244) Nervous (0.178)<br>Hematopoietic/Immune (0.167)          | Cancer (0.433) Inflammation (0.322) Fetal (0.156)            | pINCY       |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction) | Vector  |
|--------------------------|---|--|---------|
| 150                      | Cardiovascular (0.923) Developmental (0.077)                                  | Cancer (0.692) Fetal (0.154) Inflammation (0.154)            | pINCY   |
| 151                      | Reproductive (0.215) Nervous (0.190)<br>Gastrointestinal (0.177)              | Cancer (0.494) Inflammation (0.278) Trauma (0.152)           | pINCY   |
| 152                      | Reproductive (0.200) Nervous (0.171)<br>Hematopoietic/Immune (0.143)          | Inflammation (0.371) Cancer (0.229) Fetal (0.200)            | pINCY   |
| 153                      | Reproductive (0.333) Nervous (0.157)<br>Hematopoietic/Immune (0.137)          | Cancer (0.549) Inflammation (0.176) Fetal (0.137)            | pINCY   |
| 154                      | Gastrointestinal (0.500) Urologic (0.167)                                     | Inflammation (0.667) Cancer (0.167) Trauma (0.167)           | pINCY   |
| 155                      | Gastrointestinal (0.429) Reproductive (0.286)<br>Nervous (0.143)              | Inflammation (0.429) Cancer (0.286) Trauma (0.143)           | pINCY   |
| 156                      | Reproductive (1.000)  | Cancer (0.500) Inflammation (0.500)                          | pINCY   |
| 157                      | Hematopoietic/Immune (0.346) Reproductive (0.154)<br>Gastrointestinal (0.115) | Cancer (0.404) Inflammation (0.404) Fetal (0.212)            | pINCY   |
| 158                      | Reproductive (0.236) Hematopoietic/Immune (0.217)<br>Gastrointestinal (0.132) | Cancer (0.415) Inflammation (0.358) Fetal (0.142)            | pINCY   |
| 159                      | Gastrointestinal (1.000)  | Cancer (1.000)   | pSPORT1 |
| 160                      | Developmental (0.500) Hematopoietic/Immune (0.250)<br>Nervous (0.250)         | Fetal (0.500) Inflammation (0.250) Trauma (0.250)            | pINCY   |
| 161                      | Hematopoietic/Immune (0.250) Reproductive (0.250)<br>Nervous (0.208)          | Cancer (0.583) Fetal (0.292) Inflammation (0.250)            | pINCY   |
| 162                      | Gastrointestinal (0.412) Reproductive (0.412)<br>Cardiovascular (0.088)       | Cancer (0.735) Inflammation (0.176) Fetal (0.029)            | pINCY   |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction) | Vector  |
|--------------------------|---|--|---------|
| 163                      | Reproductive (0.298) Cardiovascular (0.170) Nervous<br>(0.149)                | Cancer (0.532) Inflammation (0.213) Fetal (0.191)            | pINCY   |
| 164                      | Gastrointestinal (0.333) Hematopoietic/Immune (0.333)<br>Reproductive (0.333) | Cancer (0.667) Inflammation (0.333)                          | pINCY   |
| 165                      | Reproductive (0.295) Gastrointestinal (0.159)<br>Nervous (0.148)              | Cancer (0.534) Inflammation (0.284) Fetal (0.091)            | pINCY   |
| 166                      | Hematopoietic/Immune (0.538) Cardiovascular (0.077)<br>Reproductive (0.077)   | Inflammation (0.731) Cancer (0.154) Fetal (0.154)            | pINCY   |
| 167                      | Reproductive (0.483) Gastrointestinal (0.121)<br>Nervous (0.103)              | Cancer (0.672) Inflammation (0.155)                          | pINCY   |
| 168                      | Gastrointestinal (0.222) Hematopoietic/Immune (0.222)<br>Nervous (0.148)      | Cancer (0.519) Inflammation (0.370) Fetal (0.259)            | pINCY   |
| 169                      | Urologic (1.000)  | Cancer (0.333) Fetal (0.333) Inflammation (0.333)            | pINCY   |
| 170                      | Reproductive (0.214) Gastrointestinal (0.179)<br>Nervous (0.143)              | Cancer (0.643) Inflammation (0.143) Fetal (0.107)            | pINCY   |
| 171                      | Reproductive (0.261) Developmental (0.174)<br>Nervous (0.174)                 | Cancer (0.391) Fetal (0.304) Inflammation (0.217)            | pINCY   |
| 172                      | Reproductive (0.357) Gastrointestinal (0.321)<br>Cardiovascular (0.071)       | Cancer (0.571) Inflammation (0.286) Fetal (0.107)            | pINCY   |
| 173                      | Reproductive (0.306) Nervous (0.161)<br>Cardiovascular (0.129)                | Cancer (0.387) Inflammation (0.323) Fetal (0.226)            | pINCY   |
| 174                      | Reproductive (0.229) Nervous (0.188)<br>Cardiovascular (0.167)                | Cancer (0.521) Inflammation (0.312) Trauma (0.146)           | pSPORT1 |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)                                   | Disease/Condition-Specific Expression (Total of<br>Fraction) | Vector      |
|--------------------------|---|--|-------------|
| 175                      | Reproductive (0.444) Developmental (0.167)<br>Cardiovascular (0.111)    | Cancer (0.556) Fetal (0.278) Trauma (0.111)                  | pSPORT1     |
| 176                      | Reproductive (0.294) Gastrointestinal (0.176)<br>Cardiovascular (0.118) | Cancer (0.765) Fetal (0.118) Inflammation (0.118)            | pSPORT1     |
| 177                      | Gastrointestinal (1.000)  | Cancer (0.667) Inflammation (0.333)                          | pINCY       |
| 178                      | Reproductive (0.385) Nervous (0.231)<br>Gastrointestinal (0.154)        | Cancer (0.385) Inflammation (0.385)                          | pINCY       |
| 179                      | Reproductive (0.500) Cardiovascular (0.167)<br>Gastrointestinal (0.167) | Cancer (0.667) Fetal (0.167) Inflammation (0.167)            | pBLUESCRIPT |
| 180                      | Cardiovascular (0.231) Reproductive (0.231)<br>Gastrointestinal (0.154) | Cancer (0.615) Inflammation (0.308) Fetal (0.154)            | pINCY       |
| 181                      | Reproductive (0.324) Gastrointestinal (0.176)<br>Cardiovascular (0.130) | Cancer (0.519) Inflammation (0.222) Fetal (0.157)            | pINCY       |
| 182                      | Reproductive (0.320) Nervous (0.180)<br>Gastrointestinal (0.120)        | Cancer (0.580) Inflammation (0.160) Fetal (0.100)            | pINCY       |
| 183                      | Gastrointestinal (0.667) Reproductive (0.333)                           | Cancer (1.000)   | pINCY       |
| 184                      | Urologic (0.667) Dermatologic (0.333)                                   | Cancer (0.667) Fetal (0.333)                                 | pSPORT1     |
| 185                      | Cardiovascular (0.500) Reproductive (0.500)                             | Cancer (1.000)   | pINCY       |
| 186                      | Reproductive (0.393) Developmental (0.107)<br>Urologic (0.107)          | Cancer (0.607) Fetal (0.179) Inflammation (0.107)            | pINCY       |
| 187                      | Cardiovascular (0.400) Reproductive (0.333)<br>Gastrointestinal (0.133) | Inflammation (0.467) Cancer (0.267) Fetal (0.267)            | pSPORT1     |
| 188                      | Nervous (0.318) Reproductive (0.227) Urologic (0.136)                   | Cancer (0.636) Inflammation (0.136) Trauma (0.091)           | pINCY       |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)  | Disease/Condition-Specific Expression (Total of<br>Fraction)          | Vector      |
|--------------------------|--|---|-------------|
| 189                      | Cardiovascular (0.500) Reproductive (0.500)                                      | Cancer (1.000)  | pINCY       |
| 190                      | Reproductive (0.318) Nervous (0.227)<br>Hematopoietic/Immune (0.136)             | Cancer (0.500) Fetal (0.227) Inflammation (0.227)                     | pINCY       |
| 191                      | Reproductive (0.253) Cardiovascular (0.158)<br>Gastrointestinal (0.147)          | Cancer (0.463) Inflammation (0.232) Fetal (0.200)                     | pINCY       |
| 192                      | Reproductive (0.333) Gastrointestinal (0.286)<br>Cardiovascular (0.095)          | Cancer (0.571) Inflammation (0.333) Fetal (0.095)                     | pINCY       |
| 193                      | Reproductive (0.304) Cardiovascular (0.217)<br>Gastrointestinal (0.130)          | Cancer (0.435) Inflammation (0.391) Fetal (0.174)                     | pINCY       |
| 194                      | Reproductive (0.312) Nervous (0.188)<br>Cardiovascular (0.125)                   | Cancer (0.438) Inflammation (0.250) Fetal (0.188)                     | pINCY       |
| 195                      | Developmental (1.000)  | Fetal (1.000)   | pINCY       |
| 196                      | Reproductive (0.233) Cardiovascular (0.209)<br>Nervous (0.140)                   | Cancer (0.605) Fetal (0.186) Inflammation (0.116)                     | pINCY       |
| 197                      | Reproductive (0.182) Gastrointestinal (0.136)<br>Hematopoietic/Immune (0.136)    | Cancer (0.477) Inflammation (0.341) Fetal (0.182)                     | pINCY       |
| 198                      | Gastrointestinal (0.205) Reproductive (0.205)<br>Cardiovascular (0.114)          | Inflammation (0.341) Cancer (0.250) Fetal (0.227)                     | pINCY       |
| 199                      | Cardiovascular (0.520) Reproductive (0.280)<br>Developmental (0.160)             | Cancer (0.720) Fetal (0.200) Inflammation (0.080)                     | pINCY       |
| 200                      | Lung (0.958) Developmental (0.25)<br>Musculoskeletal (0.042)                     | Cancer (0.583) Fetal or Proliferating (0.292)<br>Inflammation (0.167) | pBLUESCRIPT |
| 201                      | Reproductive (0.571) Musculoskeletal (0.143)<br>Nervous (0.143) Urologic (0.143) | Cancer (0.429) Inflammation (0.571)                                   | pSPORT1     |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)  | Disease/Condition-Specific Expression (Total of<br>Fraction)          | Vector      |
|--------------------------|--|---|-------------|
| 202                      | Endocrine (0.250) Nervous (0.250) Cardiovascular (0.125)<br>Developmental (0.125) Gastrointestinal (0.125)<br>Reproductive (0.125) | Cancer (0.375) Inflammation (0.625)<br>Fetal or Proliferating (0.125) | pSPORT1     |
| 203                      | Lung (1.000)   | Fetal or Proliferating (1.000)  | pINCY       |
| 204                      | Lung (0.500) Penis (0.500)   | Cancer (0.500)  | pINCY       |
| 205                      | Cardiovascular (0.231) Dermatologic (0.231)<br>Reproductive (0.231)  | Fetal or Proliferating (0.385) Cancer (0.308)                         | pINCY       |
| 206                      | Nervous (0.596) Reproductive (0.154)<br>Gastrointestinal (0.077)   | Cancer (0.442) Neurological (0.192)<br>Inflammation (0.231)           | pINCY       |
| 207                      | Gastrointestinal (1.000)   | Inflammation (1.000)  | pINCY       |
| 208                      | Reproductive (0.300) Hematopoietic/Immune (0.200)<br>Nervous (0.150)   | Cancer (0.450) Inflammation (0.400)<br>Fetal or Proliferating (0.250) | pSPORT1     |
| 209                      | Heart (0.500) Brain (0.500)  | Neurological (0.500) Inflammation (0.500)                             | pINCY       |
| 210                      | Nervous (0.625) Reproductive (0.250)<br>Musculoskeletal (0.125)  | Cancer (0.750) Fetal or Proliferating (0.250)<br>Neurological (0.125) | pINCY       |
| 211                      | Nervous (0.261) Reproductive (0.304)<br>Gastrointestinal (0.174)   | Cancer (0.522) Fetal or Proliferating (0.174)<br>Inflammation (0.130) | pSPORT1     |
| 212                      | Testis (1.000)   | Inflammation (1.000)  | pBLUESCRIPT |
| 213                      | Nervous (0.400) Reproductive (0.400)<br>Gastrointestinal (0.200)   | Cancer (0.400) Inflammation (0.400)<br>Neurological (0.200)           | pBLUESCRIPT |
| 214                      | Reproductive (0.476) Gastrointestinal (0.286)<br>Cardiovascular (0.095)  | Cancer (0.714) Inflammation (0.286)<br>Neurological (0.048)           | pSPORT1     |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction)          | Vector  |
|--------------------------|---|---|---------|
| 215                      | Reproductive (0.284) Gastrointestinal (0.216)<br>Nervous (0.176) Hematopoietic/Immune (0.108)<br>Cardiovascular (0.108) | Cancer (0.486) Inflammation (0.351)<br>Fetal or Proliferating (0.122) | pSPORT1 |
| 216                      | Uterus (0.500) Prostate (0.500)   | Cancer (0.500) Inflammation (0.500)                                   | pINCY   |
| 217                      | Nervous (0.429) Cardiovascular (0.143)<br>Gastrointestinal (0.143) Hematopoietic/Immune (0.143)<br>Reproductive (0.143) | Cancer (0.571) Inflammation (0.429)<br>Fetal or Proliferating (0.285) | pSPORT1 |
| 218                      | Reproductive (0.450) Hematopoietic/Immune (0.200)<br>Nervous (0.100) Gastrointestinal (0.100)                           | Cancer (0.650) Inflammation (0.200)<br>Fetal or Proliferating (0.050) | pINCY   |
| 219                      | Reproductive (0.364) Cardiovascular (0.182)<br>Nervous (0.182)  | Cancer (0.636) Fetal or Proliferating (0.182)<br>Inflammation (0.273) | pINCY   |
| 220                      | Prostate (1.000)  | Inflammation (1.000)  | pSPORT1 |
| 221                      | Developmental (0.333) Nervous (0.333)<br>Reproductive (0.333)   | Cancer (0.667) Fetal or Proliferating (0.667)                         | pSPORT1 |
| 222                      | Reproductive (0.393) Hematopoietic/Immune (0.180)<br>Nervous (0.098) Cardiovascular (0.098)                             | Cancer (0.508) Inflammation (0.344)<br>Fetal or Proliferating (0.066) | pSPORT1 |
| 223                      | Endocrine (0.333) Gastrointestinal (0.333)<br>Reproductive (0.333)  | Cancer (1.000)  | pINCY   |
| 224                      | Cardiovascular (0.200) Developmental (0.200)<br>Gastrointestinal (0.200) Reproductive (0.200)<br>Urologic (0.200)       | Cancer (0.800) Fetal or Proliferating (0.200)                         | pINCY   |
| 225                      | Lung (1.000)  | Cancer (1.000)  | pINCY   |
| 226                      | Reproductive (0.302) Hematopoietic/Immune (0.254)<br>Cardiovascular (0.111)   | Cancer (0.381) Inflammation (0.381)<br>Fetal or Proliferating (0.286) | pSPORT1 |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction)          | Vector      |
|--------------------------|---|---|-------------|
| 227                      | Lymphocytes (1.000)   | Inflammation (1.000)  | pINCY       |
| 228                      | Cardiovascular (0.531) Reproductive (0.250)<br>Urologic (0.094)   | Cancer (0.656) Inflammation (0.250)<br>Fetal or Proliferating (0.094) | pINCY       |
| 229                      | Reproductive (0.333) Cardiovascular (0.167)<br>Gastrointestinal (0.167) Endocrine (0.167)<br>Hematopoietic/Immune (0.167) | Cancer (0.500) Fetal or Proliferating (0.167)<br>Inflammation (0.333) | pINCY       |
| 230                      | Hematopoietic/Immune (0.500) Reproductive (0.500)   | Cell Proliferation (0.500)<br>Inflammation (0.500)                    | pBLUESCRIPT |
| 231                      | Cardiovascular (0.333) Nervous (0.333)<br>Developmental (0.167)   | Cancer (0.500) Cell Proliferation (0.333)<br>Inflammation (0.167)     | pINCY       |
| 232                      | Gastrointestinal (0.938) Reproductive (0.062)   | Cancer (0.500) Inflammation (0.500)                                   | pINCY       |
| 233                      | Nervous (0.324) Reproductive (0.235)<br>Hematopoietic/Immune (0.118)  | Cancer (0.456) Inflammation (0.235)<br>Trauma (0.147)                 | pINCY       |
| 234                      | Nervous (0.255) Reproductive (0.255)<br>Musculoskeletal (0.182)   | Cancer (0.545) Inflammation (0.255)<br>Trauma (0.109)                 | pINCY       |
| 235                      | Musculoskeletal (0.308) Reproductive (0.231)<br>Gastrointestinal (0.154)  | Cancer (0.538) Inflammation (0.231)<br>Trauma (0.154)                 | pINCY       |
| 236                      | Nervous (1.000)   | Cancer (1.000)  | pINCY       |
| 237                      | Gastrointestinal (0.429)<br>Hematopoietic/Immune (0.143) Nervous (0.143)  | Cancer (0.571) Cell Proliferation (0.143) Trauma (0.143)              | pINCY       |
| 238                      | Reproductive (0.254) Gastrointestinal (0.160)<br>Nervous (0.128)  | Cancer (0.453) Inflammation (0.241)<br>Cell Proliferation (0.175)     | pINCY       |
| 239                      | Nervous (0.333) Dermatologic (0.167)<br>Endocrine (0.167)   | Trauma (0.333) Cancer (0.167)<br>Cell Proliferation (0.167)           | pINCY       |



TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction)      | Vector  |
|--------------------------|---|---|---------|
| 240                      | Nervous (0.273) Reproductive (0.227)<br>Endocrine (0.136)                       | Cancer (0.545) Cell Proliferation (0.182)<br>Inflammation (0.182) | pINCY   |
| 241                      | Reproductive (0.273)<br>Hematopoietic/Immune (0.182) Urologic (0.182)           | Cancer (0.455) Cell Proliferation (0.273)<br>Inflammation (0.273) | pINCY   |
| 242                      | Endocrine (1.000)   | Trauma (1.000)  | pSPORT1 |
| 243                      | Reproductive (1.000)  | Cancer (1.000)  | pINCY   |
| 244                      | Hematopoietic/Immune (0.545)<br>Musculoskeletal (0.182) Cardiovascular (0.091)  | Inflammation (0.636) Trauma (0.182)<br>Cancer (0.091)             | pINCY   |
| 245                      | Hematopoietic/Immune (0.400)<br>Musculoskeletal (0.300) Cardiovascular (0.150)  | Inflammation (0.650) Cancer (0.300)                               | pINCY   |
| 246                      | Urologic (1.000)  | Cancer (0.500) Cell Proliferation (0.500)                         | pINCY   |
| 247                      | Nervous (0.292) Reproductive (0.222)<br>Musculoskeletal (0.125)                 | Cell Proliferation (0.625) Inflammation/Trauma (0.181)            | pSPORT1 |
| 248                      | Reproductive (0.211) Developmental (0.132)<br>Nervous (0.132)                   | Cell Proliferation (0.658) Inflammation/Trauma (0.184)            | pSPORT1 |
| 249                      | Nervous (0.500) Gastrointestinal (0.300)<br>Hematopoietic/Immune (0.100)        | Cell Proliferation (0.900) Inflammation/Trauma (0.300)            | pSPORT1 |
| 250                      | Cardiovascular (0.209) Gastrointestinal (0.140)<br>Hematopoietic/Immune (0.140) | Cell Proliferation (0.605) Inflammation/Trauma (0.256)            | pINCY   |
| 251                      | Nervous (0.308) Cardiovascular (0.154)<br>Gastrointestinal (0.154)              | Cell Proliferation (0.616) Inflammation/Trauma (0.269)            | pINCY   |
| 252                      | Reproductive (1.000)  | Cell Proliferation (1.000)  | pSPORT1 |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction) | Vector      |
|--------------------------|---|--|-------------|
| 253                      | Reproductive (0.324) Nervous (0.162)<br>Gastrointestinal (0.113)              | Cell Proliferation (0.641) Inflammation/Trauma (0.197)       | pSPORT1     |
| 254                      | Reproductive (0.315) Nervous (0.296)<br>Developmental (0.093)                 | Cell Proliferation (0.630) Inflammation/Trauma (0.278)       | pSPORT1     |
| 255                      | Nervous (0.211) Reproductive (0.211)<br>Gastrointestinal (0.158)              | Cell Proliferation (0.579) Inflammation/Trauma (0.298)       | pINCY       |
| 256                      | Reproductive (0.250) Gastrointestinal (0.148)<br>Hematopoietic/Immune (0.148) | Cell Proliferation (0.705) Inflammation/Trauma (0.193)       | pINCY       |
| 257                      | Hematopoietic/Immune (1.000)  | Cell Proliferation (0.400) Inflammation/Trauma (0.600)       | pINCY       |
| 258                      | Cardiovascular (0.333) Reproductive (0.333)<br>Developmental (0.167)          | Cell Proliferation (0.833) Inflammation/Trauma (0.333)       | pBLUESCRIPT |
| 259                      | Cardiovascular (0.333) Reproductive (0.250)<br>Developmental (0.167)          | Cell Proliferation (0.625) Inflammation/Trauma (0.208)       | pINCY       |
| 260                      | Endocrine (0.500) Cardiovascular (0.250) Nervous (0.250)                      | Cell Proliferation (0.750) Inflammation/Trauma (0.500)       | pINCY       |
| 261                      | Reproductive (0.252) Cardiovascular (0.155)<br>Hematopoietic/Immune (0.136)   | Cell Proliferation (0.728) Inflammation/Trauma (0.194)       | pINCY       |
| 262                      | Reproductive (0.274) Cardiovascular (0.177)<br>Nervous (0.145)                | Cell Proliferation (0.742) Inflammation/Trauma (0.210)       | pINCY       |
| 263                      | Reproductive (0.267) Cardiovascular (0.160)<br>Hematopoietic/Immune (0.127)   | Cell Proliferation (0.654) Inflammation/Trauma (0.193)       | pINCY       |
| 264                      | Nervous (0.229) Hematopoietic/Immune (0.200)<br>Reproductive (0.200)          | Cell Proliferation (0.743) Inflammation/Trauma (0.286)       | pINCY       |
| 265                      | Hematopoietic/Immune (0.333) Gastrointestinal (0.167)<br>Nervous (0.133)      | Cell Proliferation (0.600) Inflammation/Trauma (0.333)       | pINCY       |

TABLE 3 (cont.)

| Nucleotide<br>SEQ ID NO: | Tissue Expression (Fraction of Total)   | Disease/Condition-Specific Expression (Total of<br>Fraction) | Vector  |
|--------------------------|---|--|---------|
| 266                      | Nervous (0.290) Reproductive (0.258)<br>Cardiovascular (0.129)                | Cell Proliferation (0.677) Inflammation/Trauma (0.194)       | pINCY   |
| 267                      | Reproductive (0.261) Hematopoietic/Immune (0.217)<br>Cardiovascular (0.087)   | Cell Proliferation (0.652) Inflammation/Trauma (0.391)       | pINCY   |
| 268                      | Gastrointestinal (0.227) Reproductive (0.193)<br>Hematopoietic/Immune (0.168) | Cell Proliferation (0.731) Inflammation/Trauma (0.227)       | pSPORT1 |

TABLE 4

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library    | Library Description  |
|------------------------------|----------|------------|--|
| 135                          | 443531   | MPHGNOT03  | The library was constructed using RNA isolated from plastic adherent mononuclear cells isolated from buffy coat units obtained from unrelated male and female donors.  |
| 136                          | 632860   | NEUTGMT01  | The library was constructed using RNA isolated from peripheral blood granulocytes collected by density gradient centrifugation through Ficoll-Hypaque. The cells were isolated from buffy coat units obtained from 20 unrelated male and female donors. Cells were cultured in 10 nM GM-CSF for 1 hour before washing and harvesting for RNA preparation.  |
| 137                          | 670010   | CRBLNOT01  | The library was constructed using RNA isolated from the cerebellum tissue of a 69-year-old Caucasian male who died from chronic obstructive pulmonary disease. Patient history included myocardial infarction, hypertension, and osteoarthritis.   |
| 138                          | 726498   | SYNOOA T01 | The library was constructed using RNA isolated from the knee synovial membrane tissue of an 82-year-old female with osteoarthritis.  |
| 139                          | 795064   | OVARNOT03  | The library was constructed using RNA isolated from ovarian tissue removed from a 43-year-old Caucasian female during removal of the fallopian tubes and ovaries. Pathology for the associated tumor tissue indicated grade 2 mucinous cystadenocarcinoma. Patient history included mitral valve disorder, pneumonia, and viral hepatitis. Family history included atherosclerotic coronary artery disease, pancreatic cancer, cerebrovascular disease, breast cancer, and uterine cancer. |
| 140                          | 924925   | BRAINOT04  | The library was constructed using RNA isolated from the brain tissue of a 44-year-old Caucasian male with a cerebral hemorrhage. The tissue, which contained coagulated blood, came from the choroid plexus of the right anterior temporal lobe. Family history included coronary artery disease and myocardial infarction.  |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 141                          | 962390   | BRSTTUT03 | The library was constructed using RNA isolated from breast tumor tissue removed from a 58-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated multicentric invasive grade 4 lobular carcinoma. The mass was identified in the upper outer quadrant, and three separate nodules were found in the lower outer quadrant of the left breast. Patient history included skin cancer, rheumatic heart disease, osteoarthritis, and tuberculosis. Family history included cerebrovascular disease, coronary artery aneurysm, breast cancer, prostate cancer, atherosclerotic coronary artery disease, and type I diabetes. |
| 142                          | 1259405  | MENITUT03 | The library was constructed using RNA isolated from brain meningioma tissue removed from a 35-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated a benign neoplasm in the right cerebellopontine angle of the brain. Patient history included hypothyroidism. Family history included myocardial infarction and breast cancer.   |
| 143                          | 1297384  | BRSTNOT07 | The library was constructed using RNA isolated from diseased breast tissue removed from a 43-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated mildly proliferative fibrocystic changes with epithelial hyperplasia, papillomatosis, and duct ectasia. Pathology for the associated tumor tissue indicated invasive grade 4, nuclear grade 3 mammary adenocarcinoma with extensive comedo necrosis. Family history included epilepsy, atherosclerotic coronary artery disease, and type II diabetes.  |
| 144                          | 1299627  | BRSTNOT07 | The library was constructed using RNA isolated from diseased breast tissue removed from a 43-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated mildly proliferative fibrocystic changes with epithelial hyperplasia, papillomatosis, and duct ectasia. Pathology for the associated tumor tissue indicated invasive grade 4, nuclear grade 3 mammary adenocarcinoma with extensive comedo necrosis. Family history included epilepsy, atherosclerotic coronary artery disease, and type II diabetes.  |
| 145                          | 1306026  | PLACNOT02 | The library was constructed using RNA isolated from the placental tissue of a Hispanic female fetus, who was prematurely delivered at 21 weeks' gestation. Serologies of the mother's blood were positive for CMV (cytomegalovirus).  |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 146                          | 1316219  | BLADTUT02 | The library was constructed using RNA isolated from bladder tumor tissue removed from an 80-year-old Caucasian female during a radical cystectomy and lymph node excision. Pathology indicated grade 3 invasive transitional cell carcinoma. Family history included osteoarthritis and atherosclerosis.   |
| 147                          | 1329031  | PANCNOT07 | The library was constructed using RNA isolated from the pancreatic tissue of a Caucasian male fetus, who died at 23 weeks' gestation.  |
| 148                          | 1483050  | CORPNOT02 | The library was constructed using RNA isolated from diseased corpus callosum tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.  |
| 149                          | 1514160  | PANCTUT01 | The library was constructed using RNA isolated from pancreatic tumor tissue removed from a 65-year-old Caucasian female during radical subtotal pancreatectomy. Pathology indicated an invasive grade 2 adenocarcinoma. Patient history included type II diabetes, osteoarthritis, cardiovascular disease, benign neoplasm in the large bowel, and a cataract. Family history included cardiovascular disease, type II diabetes, and stomach cancer.   |
| 150                          | 1603403  | LUNGNOT15 | The library was constructed using RNA isolated from lung tissue removed from a 69-year-old Caucasian male during a segmental lung resection. Pathology for the associated tumor tissue indicated residual grade 3 invasive squamous cell carcinoma. Patient history included acute myocardial infarction, prostatic hyperplasia, and malignant skin neoplasm. Family history included cerebrovascular disease, type I diabetes, acute myocardial infarction, and arteriosclerotic coronary disease.                    |
| 151                          | 1652303  | PROSTUT08 | The library was constructed using RNA isolated from prostate tumor tissue removed from a 60-year-old Caucasian male during radical prostatectomy and regional lymph node excision. Pathology indicated an adenocarcinoma (Gleason grade 3+4). Adenofibromatous hyperplasia was also present. The patient presented with elevated prostate specific antigen (PSA). Patient history included a kidney cyst. Family history included tuberculosis, cerebrovascular disease, and arteriosclerotic coronary artery disease. |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 152                          | 1693358  | COLNNOT23 | The library was constructed using RNA isolated from diseased colon tissue removed from a 16-year-old Caucasian male during a total colectomy with abdominal/perineal resection. Pathology indicated gastritis and pancolitis consistent with the acute phase of ulcerative colitis. There was only mild involvement of the ascending and sigmoid colon, and no significant involvement of the cecum, rectum, or terminal ileum. Family history included irritable bowel syndrome.  |
| 153                          | 1707711  | DUODNOT02 | The library was constructed using RNA isolated from duodenal tissue of a 8-year-old Caucasian female, who died from head trauma. Serology was positive for cytomegalovirus (CMV).  |
| 154                          | 1738735  | COLNNOT22 | The library was constructed using RNA isolated from colon tissue removed from a 56-year-old Caucasian female with Crohn's disease during a partial resection of the small intestine. Pathology indicated Crohn's disease of the ileum and ileal-colonic anastomosis, causing a fistula at the anastomotic site that extended into pericolic fat. The ileal mucosa showed linear and punctate ulcers with intervening normal tissue. Previous surgeries included a partial ileal resection and permanent ileostomy. Family history included irritable bowel syndrome. |
| 155                          | 1749147  | STOMTUT02 | The library was constructed using RNA isolated from stomach tumor tissue obtained from a 68-year-old Caucasian female during a partial gastrectomy. Pathology indicated a malignant lymphoma of diffuse large-cell type. Patient history included thalassemia. Family history included acute leukemia, malignant neoplasm of the esophagus, malignant stomach neoplasm, and atherosclerotic coronary artery disease.   |
| 156                          | 1817722  | PROSNOT20 | The library was constructed using RNA isolated from diseased prostate tissue removed from a 65-year-old Caucasian male during a radical prostatectomy. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma.  |
| 157                          | 1831290  | THP1AZT01 | The library was constructed using 1 microgram of poly(A) RNA isolated from THP-1 promonocyte cells treated for three days with 0.8 micromolar 5-aza-2'-deoxycytidine. THP-1 (ATCC TIB 202) is a human promonocyte line derived from peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 158                          | 1831477  | THPIAZT01 | The library was constructed using 1 microgram of polyA RNA isolated from THP-1 promonocyte cells treated for three days with 0.8 micromolar 5-aza-2'-deoxycytidine. THP-1 (ATCC TIB 202) is a human promonocyte line derived from peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.  |
| 159                          | 1841607  | COLNNOT07 | The library was constructed using RNA isolated from colon tissue removed from a 60-year-old Caucasian male during a left hemicolectomy.   |
| 160                          | 1852391  | LUNGFET03 | The library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.   |
| 161                          | 1854555  | HNT3AZT01 | Library was constructed using RNA isolated from the hNT2 cell line (derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor). Cells were treated for three days with 0.35 micromolar 5-aza-2'-deoxycytidine (AZT).  |
| 162                          | 1855755  | PROSNOT18 | The library was constructed using RNA isolated from diseased prostate tissue removed from a 58-year-old Caucasian male during a radical cystectomy, radical prostatectomy, and gastrectomy. Pathology indicated adenofibromatous hyperplasia. This tissue was associated with a grade 3 transitional cell carcinoma. Patient history included angina and emphysema. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.   |
| 163                          | 1861434  | PROSNOT19 | The library was constructed using RNA isolated from diseased prostate tissue removed from a 59-year-old Caucasian male during a radical prostatectomy with regional lymph node excision. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated an adenocarcinoma (Gleason grade 3+3). The patient presented with elevated prostate-specific antigen (PSA). Patient history included colon diverticuli and thrombophlebitis. Family history included benign hypertension, multiple myeloma, hyperlipidemia and rheumatoid arthritis. |
| 164                          | 1872334  | LEUKNOT02 | The library was constructed using RNA isolated from white blood cells of a 45-year-old female with blood type O+. The donor tested positive for cytomegalovirus (CMV).  |
| 165                          | 1877230  | LEUKNOT03 | The library was constructed using RNA isolated from white blood cells of a 27-year-old female with blood type A+. The donor tested negative for cytomegalovirus (CMV).  |



TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 166                          | 1877885  | LEUKNOT03 | The library was constructed using RNA isolated from white blood cells of a 27-year-old female with blood type A+. The donor tested negative for cytomegalovirus (CMV).   |
| 167                          | 1889269  | BLADTUT07 | The library was constructed using RNA isolated from bladder tumor tissue removed from the anterior bladder wall of a 58-year-old Caucasian male during a radical cystectomy, radical prostatectomy, and gastrectomy. Pathology indicated a grade 3 transitional cell carcinoma in the left lateral bladder. Patient history included angina and emphysema. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.     |
| 168                          | 1890243  | BLADTUT07 | The library was constructed using RNA isolated from bladder tumor tissue removed from the anterior bladder wall of a 58-year-old Caucasian male during a radical cystectomy, radical prostatectomy, and gastrectomy. Pathology indicated a grade 3 transitional cell carcinoma in the left lateral bladder. Patient history included angina and emphysema. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes.     |
| 169                          | 1900433  | BLADTUT06 | The library was constructed using RNA isolated from bladder tumor tissue removed from the posterior bladder wall of a 58-year-old Caucasian male during a radical cystectomy, radical prostatectomy, and gastrectomy. Pathology indicated grade 3 transitional cell carcinoma in the left lateral bladder wall. Patient history included angina and emphysema. Family history included acute myocardial infarction, atherosclerotic coronary artery disease, and type II diabetes. |
| 170                          | 1909441  | CONNTUT01 | The library was constructed using RNA isolated from a soft tissue tumor removed from the clival area of the skull of a 30-year-old Caucasian female. Pathology indicated chondroid chordoma with neoplastic cells reactive for keratin.  |
| 171                          | 1932226  | COLNNOT16 | The library was constructed using RNA isolated from sigmoid colon tissue removed from a 62-year-old Caucasian male during a sigmoidectomy and permanent colostomy.   |
| 172                          | 1932647  | COLNNOT16 | The library was constructed using RNA isolated from sigmoid colon tissue removed from a 62-year-old Caucasian male during a sigmoidectomy and permanent colostomy.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 173                          | 2124245  | BRSTNOT07 | The library was constructed using RNA isolated from diseased breast tissue removed from a 43-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated mildly proliferative fibrocystic changes with epithelial hyperplasia, papillomatosis, and duct ectasia. Pathology for the associated tumor tissue indicated invasive grade 4, nuclear grade 3 mammary adenocarcinoma with extensive comedo necrosis. Family history included epilepsy, atherosclerotic coronary artery disease, and type II diabetes. |
| 174                          | 2132626  | OVARNOT03 | The library was constructed using RNA isolated from ovarian tissue removed from a 43-year-old Caucasian female during removal of the fallopian tubes and ovaries. Pathology for the associated tumor tissue indicated grade 2 mucinous cystadenocarcinoma. Patient history included mitral valve disorder, pneumonia, and viral hepatitis. Family history included atherosclerotic coronary artery disease, pancreatic cancer, cerebrovascular disease, breast cancer, and uterine cancer.   |
| 175                          | 2280639  | PROSNON01 | The library was constructed and normalized from 4.4 million independent clones from the PROSNOT11 library. Starting RNA was made from prostate tissue removed from a 28-year-old Caucasian male who died from a gunshot wound. The normalization and hybridization conditions were adapted from Soares, M.B. et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228-9232, using a longer (19 hour) reannealing hybridization period.   |
| 176                          | 2292356  | BRAINON01 | The library was constructed and normalized from 4.88 million independent clones from the BRAINOT03 library. Starting RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.  |
| 177                          | 2349310  | COLSUCT01 | The library was constructed using RNA isolated from diseased sigmoid colon tissue obtained from a 70-year-old Caucasian male during colectomy with permanent ileostomy. Pathology indicated chronic ulcerative colitis. Patient history included benign neoplasm of the colon. Family history included atherosclerotic coronary artery disease and myocardial infarctions.   |
| 178                          | 2373227  | ADRENOT07 | The library was constructed using RNA isolated from adrenal tissue removed from a 61-year-old female during a bilateral adrenalectomy. Patient history included an unspecified disorder of the adrenal glands.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 179                          | 2457682  | ENDANOT01 | The library was constructed using RNA isolated from aortic endothelial cell tissue from an explanted heart removed from a male during a heart transplant.  |
| 180                          | 2480426  | SMCANOT01 | The library was constructed using RNA isolated from an aortic smooth muscle cell line derived from the explanted heart of a male during a heart transplant.  |
| 181                          | 2503743  | CONUTUT01 | The library was constructed using RNA isolated from sigmoid mesentery tumor tissue obtained from a 61-year-old female during a total abdominal hysterectomy and bilateral salpingo-oophorectomy with regional lymph node excision. Pathology indicated a metastatic grade 4 malignant mixed müllerian tumor present in the sigmoid mesentery at two sites.   |
| 182                          | 2537684  | BONRTUT01 | The library was constructed using RNA isolated from rib tumor tissue removed from a 16-year-old Caucasian male during a rib osteotomy and a wedge resection of the lung. Pathology indicated a metastatic grade 3 (of 4) osteosarcoma, forming a mass involving the chest wall.  |
| 183                          | 2593853  | OVARTUT02 | The library was constructed using RNA isolated from ovarian tumor tissue removed from a 51-year-old Caucasian female during an exploratory laparotomy, total abdominal hysterectomy, salpingo-oophorectomy, and an incidental appendectomy. Pathology indicated mucinous cystadenoma presenting as a multiloculated neoplasm involving the entire left ovary. The right ovary contained a follicular cyst and a hemorrhagic corpus luteum. The uterus showed proliferative endometrium and a single intramural leiomyoma. The peritoneal biopsy indicated benign glandular inclusions consistent with endosalpingiosis. Family history included atherosclerotic coronary artery disease, benign hypertension, breast cancer, and uterine cancer. |
| 184                          | 2622354  | KERANOT02 | The library was constructed using RNA isolated from epidermal breast keratinocytes (NHEK). NHEK (Clontech #CC-2501) is a human breast keratinocyte cell line derived from a 30-year-old black female during breast-reduction surgery.  |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 185                          | 2641377  | LUNGTUT08 | The library was constructed using RNA isolated from lung tumor tissue removed from a 63-year-old Caucasian male during a right upper lobectomy with fiberoptic bronchoscopy. Pathology indicated a grade 3 adenocarcinoma. Patient history included atherosclerotic coronary artery disease, an acute myocardial infarction, rectal cancer, an asymptomatic abdominal aortic aneurysm, and cardiac dysrhythmia. Family history included congestive heart failure, stomach cancer, and lung cancer, type II diabetes, atherosclerotic coronary artery disease, and an acute myocardial infarction.   |
| 186                          | 2674857  | KIDNNOT19 | The library was constructed using RNA isolated from kidney tissue removed a 65-year-old Caucasian male during an exploratory laparotomy and nephroureterectomy. Pathology for the associated tumor tissue indicated a grade I renal cell carcinoma within the upper pole of the left kidney. Patient history included malignant melanoma of the abdominal skin, benign neoplasm of colon, cerebrovascular disease, and umbilical hernia. Family history included myocardial infarction, atherosclerotic coronary artery disease, cerebrovascular disease, prostate cancer, myocardial infarction, and atherosclerotic coronary artery disease.  |
| 187                          | 2758485  | THP1AZS08 | The subtracted THP-1 promonocyte cell line library was constructed using 5.76 million clones from a 5-aza-2'-deoxycytidine (AZT) treated THP-1 cell library. Starting RNA was made from THP-1 promonocyte cells treated for three days with 0.8 micromolar AZT. The library was oligo(dT)-primed, and cDNAs were cloned directionally into the pSPORT1 vectoring system using SalI (5') and NotI (3'). The hybridization probe for subtraction was derived from a similarly constructed library, made from 1 microgram of polyA RNA isolated from untreated THP-1 cells. 5.76 million clones from the AZ-treated THP-1 cell library were then subjected to two rounds of subtractive hybridization with 5 million clones from the untreated THP-1 cell library. Subtractive hybridization conditions were based on the methodologies of Swaroop et al. (Nucl. Acids Res. (1991) 19:1954) and Bonaldo et al. (Genome Res (1996) 6: 791-806). |
| 188                          | 2763296  | BRSTNOT12 | The library was constructed using RNA isolated from diseased breast tissue removed from a 32-year-old Caucasian female during a bilateral reduction mastoplasmy. Pathology indicated nonproliferative fibrocystic disease. Family history included benign hypertension and atherosclerotic coronary artery disease.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 189                          | 2779436  | OVARTUT03 | The library was constructed using RNA isolated from ovarian tumor tissue removed from the left ovary of a 52-year-old mixed ethnicity female during a total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal and lymphatic structure biopsy, regional lymph node excision, and peritoneal tissue destruction. Pathology indicated an invasive grade 3 (of 4) seroanaplastic carcinoma forming a mass in the left ovary. The endometrium was atrophic. Multiple (2) leiomyomata were identified, one subserosal and 1 intramural. Pathology also indicated a metastatic grade 3 seroanaplastic carcinoma involving the omentum, cul-de-sac peritoneum, left broad ligament peritoneum, and mesentery colon. Patient history included breast cancer, chronic peptic ulcer, and joint pain. Family history included colon cancer, cerebrovascular disease, breast cancer, type II diabetes, esophagus cancer, and depressive disorder. |
| 190                          | 2808528  | BLADTUT08 | The library was constructed using RNA isolated from bladder tumor tissue removed from a 72-year-old Caucasian male during a radical cystectomy and prostatectomy. Pathology indicated an invasive grade 3 (of 3) transitional cell carcinoma in the right bladder base. Family history included myocardial infarction, cerebrovascular disease, brain cancer, and myocardial infarction.   |
| 191                          | 2809230  | BLADTUT08 | The library was constructed using RNA isolated from bladder tumor tissue removed from a 72-year-old Caucasian male during a radical cystectomy and prostatectomy. Pathology indicated an invasive grade 3 (of 3) transitional cell carcinoma in the right bladder base. Patient history included pure hypercholesterolemia and tobacco abuse. Family history included myocardial infarction, cerebrovascular disease, brain cancer, and myocardial infarction.   |
| 192                          | 2816821  | BRSTNOT14 | The library was constructed using RNA isolated from breast tissue removed from a 62-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated an invasive grade 3 (of 4), nuclear grade 3 (of 3) adenocarcinoma, ductal type. Ductal carcinoma in situ, comedo type, comprised 60% of the tumor mass. Metastatic adenocarcinoma was identified in one (of 14) axillary lymph nodes with no perinodal extension. The tumor cells were strongly positive for estrogen receptors and weakly positive for progesterone receptors. Patient history included a benign colon neoplasm, hyperlipidemia, and cardiac dysrhythmia. Family history included atherosclerotic coronary artery disease, myocardial infarction, colon cancer, ovarian cancer, lung cancer, and cerebrovascular disease.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 193                          | 2817268  | BRSTNOT14 | The library was constructed using RNA isolated from breast tissue removed from a 62-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated an invasive grade 3 (of 4), nuclear grade 3 (of 3) adenocarcinoma, ductal type. Ductal carcinoma in situ, comedo type, comprised 60% of the tumor mass. Metastatic adenocarcinoma was identified in one (of 14) axillary lymph nodes with no perinodal extension. The tumor cells were strongly positive for estrogen receptors and weakly positive for progesterone receptors. Patient history included a benign colon neoplasm, hyperlipidemia, and cardiac dysrhythmia. Family history included atherosclerotic coronary artery disease, myocardial infarction, colon cancer, ovarian cancer, lung cancer, and cerebrovascular disease. |
| 194                          | 2923165  | SININOT04 | The library was constructed using RNA isolated from diseased ileum tissue obtained from a 26-year-old Caucasian male during a partial colectomy, permanent colostomy, and an incidental appendectomy. Pathology indicated moderately to severely active Crohn's disease. Family history included enteritis of the small intestine.   |
| 195                          | 2949822  | KIDNFET01 | The library was constructed using RNA isolated from kidney tissue removed from a Caucasian female fetus, who died at 17 weeks' gestation from anencephalus.  |
| 196                          | 2992192  | KIDNFET02 | The library was constructed using RNA isolated from kidney tissue removed from a Caucasian male fetus, who was stillborn with a hypoplastic left heart and died at 23 weeks' gestation.  |
| 197                          | 2992458  | KIDNFET02 | The library was constructed using RNA isolated from kidney tissue removed from a Caucasian male fetus, who was stillborn with a hypoplastic left heart and died at 23 weeks' gestation.  |
| 198                          | 3044710  | HEAANOT01 | The library was constructed using RNA isolated from right coronary and right circumflex coronary artery tissue removed from the explanted heart of a 46-year-old Caucasian male during a heart transplantation. Patient history included myocardial infarction from total occlusion of the left anterior descending coronary artery, atherosclerotic coronary artery disease, hyperlipidemia, myocardial ischemia, dilated cardiomyopathy, and left ventricular dysfunction. Previous surgeries included cardiac catheterization. Family history included atherosclerotic coronary artery disease.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 199                          | 3120415  | LUNGTUT13 | The library was constructed using RNA isolated from tumorous lung tissue removed from the right upper lobe of a 47-year-old Caucasian male during a segmental lung resection. Pathology indicated invasive grade 3 (of 4) adenocarcinoma. Family history included atherosclerotic coronary artery disease, and type II diabetes.  |
| 200                          | 126758   | LUNGNOT01 | The library was constructed at Stratagene using RNA isolated from the lung tissue of a 72-year-old male.  |
| 201                          | 674760   | CRBLNOT01 | The library was constructed using RNA isolated from the cerebellum tissue of a 69-year-old Caucasian male who died from chronic obstructive pulmonary disease. Patient history included myocardial infarction, hypertension, and osteoarthritis.  |
| 202                          | 1229438  | BRAITUT01 | The library was constructed using RNA isolated from brain tumor tissue removed from a 50-year-old Caucasian female during a frontal lobectomy. Pathology indicated recurrent grade 3 oligoastrocytoma with focal necrosis and extensive calcification. Patient history included a speech disturbance and epilepsy. The patient's brain had also been irradiated with a total dose of 5,082 cGy (Fraction 8). Family history included a brain tumor.   |
| 203                          | 1236935  | LUNGFET03 | The library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus who died at 20 weeks' gestation.  |
| 204                          | 1359283  | LUNGNOT12 | The library was constructed using RNA isolated from lung tissue removed from a 78-year-old Caucasian male during a segmental lung resection and regional lymph node resection. Pathology indicated fibrosis pleura was puckered, but not invaded. Pathology for the associated tumor tissue indicated an invasive pulmonary grade 3 adenocarcinoma. Patient history included cerebrovascular disease, arteriosclerotic coronary artery disease, thrombophlebitis, chronic obstructive pulmonary disease, and asthma. Family history included intracranial hematoma, cerebrovascular disease, arteriosclerotic coronary artery disease, and type I diabetes. |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 205                          | 1450703  | PENITUT01 | The library was constructed using RNA isolated from tumor tissue removed from the penis of a 64-year-old Caucasian male during penile amputation. Pathology indicated a fungating invasive grade 4 squamous cell carcinoma involving the inner wall of the foreskin and extending onto the glans penis. Patient history included benign neoplasm of the large bowel, atherosclerotic coronary artery disease, angina pectoris, gout, and obesity. Family history included malignant pharyngeal neoplasm, chronic lymphocytic leukemia, and chronic liver disease. |
| 206                          | 1910668  | CONNTUT01 | The library was constructed using RNA isolated from a soft tissue tumor removed from the clival area of the skull of a 30-year-old Caucasian female. Pathology indicated chondroid chordoma with neoplastic cells reactive for keratin.   |
| 207                          | 1955143  | CONNNOT01 | The library was constructed using RNA isolated from mesentery fat tissue obtained from a 71-year-old Caucasian male during a partial colectomy and permanent colostomy. Family history included atherosclerotic coronary artery disease, myocardial infarction, and extrinsic asthma.   |
| 208                          | 1961637  | BRSTNOT04 | The library was constructed using RNA isolated from breast tissue removed from a 62-year-old East Indian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated an invasive grade 3 ductal carcinoma. Patient history included benign hypertension, hyperlipidemia, and hematuria. Family history included cerebrovascular and cardiovascular disease, hyperlipidemia, and liver cancer.  |
| 209                          | 1990762  | CORPNOT02 | The library was constructed using RNA isolated from diseased corpus callosum tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.   |
| 210                          | 1994131  | CORPNOT02 | The library was constructed using RNA isolated from diseased corpus callosum tissue removed from the brain of a 74-year-old Caucasian male who died from Alzheimer's disease.   |



TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 211                          | 1997745  | BRSTTUT03 | The library was constructed using RNA isolated from breast tumor tissue removed from a 58-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated multicentric invasive grade 4 lobular carcinoma. The mass was identified in the upper outer quadrant, and three separate nodules were found in the lower outer quadrant of the left breast. Patient history included skin cancer, rheumatic heart disease, osteoarthritis, and tuberculosis. Family history included cerebrovascular disease, coronary artery aneurysm, breast cancer, prostate cancer, atherosclerotic coronary artery disease, and type 1 diabetes. |
| 212                          | 2009035  | TESTNOT03 | The library was constructed using polyA RNA isolated from testicular tissue removed from a 37-year-old Caucasian male who died from liver disease. Patient history included cirrhosis, jaundice, and liver failure.   |
| 213                          | 2009152  | TESTNOT03 | The library was constructed using polyA RNA isolated from testicular tissue removed from a 37-year-old Caucasian male who died from liver disease. Patient history included cirrhosis, jaundice, and liver failure.   |
| 214                          | 2061752  | OVARNOT03 | The library was constructed using RNA isolated from ovarian tissue removed from a 43-year-old Caucasian female during removal of the fallopian tubes and ovaries. Pathology for the associated tumor tissue indicated grade 2 mucinous cystadenocarcinoma. Patient history included mitral valve disorder, pneumonia, and viral hepatitis. Family history included atherosclerotic coronary artery disease, pancreatic cancer, stress reaction, cerebrovascular disease, breast cancer, and uterine cancer.   |
| 215                          | 2061933  | OVARNOT03 | The library was constructed using RNA isolated from ovarian tissue removed from a 43-year-old Caucasian female during removal of the fallopian tubes and ovaries. Pathology for the associated tumor tissue indicated grade 2 mucinous cystadenocarcinoma. Patient history included mitral valve disorder, pneumonia, and viral hepatitis. Family history included atherosclerotic coronary artery disease, pancreatic cancer, stress reaction, cerebrovascular disease, breast cancer, and uterine cancer.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 216                          | 2081422  | UTRSNOT08 | The library was constructed using RNA isolated from uterine tissue removed from a 35-year-old Caucasian female during a vaginal hysterectomy with dilation and curettage. Pathology indicated that the endometrium was secretory phase with a benign endometrial polyp 1 cm in diameter. The cervix showed mild chronic cervicitis. Family history included atherosclerotic coronary artery disease and type II diabetes.   |
| 217                          | 2101278  | BRAITUT02 | The library was constructed using RNA isolated from brain tumor tissue removed from the frontal lobe of a 58-year-old Caucasian male during excision of a cerebral meningeal lesion. Pathology indicated a grade 2 metastatic hypernephroma. Patient history included a grade 2 renal cell carcinoma, insomnia, and chronic airway obstruction. Family history included a malignant neoplasm of the kidney.   |
| 218                          | 2121353  | BRSTNOT07 | The library was constructed using RNA isolated from diseased breast tissue removed from a 43-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated mildly proliferative fibrocystic changes with epithelial hyperplasia, papillomatosis, and duct ectasia. Pathology for the associated tumor tissue indicated invasive grade 4, nuclear grade 3 mammary adenocarcinoma with extensive comedo necrosis. Family history included epilepsy, cardiovascular disease, and type II diabetes. |
| 219                          | 2241736  | PANCTUT02 | The library was constructed using RNA isolated from pancreatic tumor tissue removed from a 45-year-old Caucasian female during radical pancreaticoduodenectomy. Pathology indicated a grade 4 anaplastic carcinoma. Family history included benign hypertension, hyperlipidemia and atherosclerotic coronary artery disease.  |
| 220                          | 2271935  | PROSNON01 | This normalized prostate library was constructed from 4.4 M independent clones from the PROSNOT11 library. Starting RNA was made from prostate tissue removed from a 28-year-old Caucasian male who died from a self-inflicted gunshot wound. The normalization and hybridization conditions were adapted from Soares, M.B. et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228-9232, using a longer (19 hour) reannealing hybridization period.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 221                          | 2295344  | BRSTNOT05 | The library was constructed using RNA isolated from breast tissue removed from a 58-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated multicentric invasive grade 4 lobular carcinoma. Patient history included skin cancer, rheumatic heart disease, osteoarthritis, and tuberculosis. Family history included cerebrovascular and cardiovascular disease, breast and prostate cancer, and type I diabetes.  |
| 222                          | 2303994  | BRSTNOT05 | The library was constructed using RNA isolated from breast tissue removed from a 58-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated multicentric invasive grade 4 lobular carcinoma. Patient history included skin cancer, rheumatic heart disease, osteoarthritis, and tuberculosis. Family history included cerebrovascular and cardiovascular disease, breast and prostate cancer, and type I diabetes.  |
| 223                          | 2497805  | ADRETUT05 | The library was constructed RNA isolated from adrenal tumor tissue removed from a 52-year-old Caucasian female during a unilateral adrenalectomy. Pathology indicated a pheochromocytoma.   |
| 224                          | 2646362  | LUNGTUT11 | The library was constructed using RNA isolated from lung tumor tissue removed from the right lower lobe a 57-year-old Caucasian male during a segmental lung resection. Pathology indicated an infiltrating grade 4 squamous cell carcinoma. Multiple intrapulmonary peribronchial lymph nodes showed metastatic squamous cell carcinoma. Patient history included a benign brain neoplasm and tobacco abuse. Family history included spinal cord cancer, type II diabetes, cerebrovascular disease, and malignant prostate neoplasm. |
| 225                          | 2657146  | LUNGTUT09 | The library was constructed using RNA isolated from lung tumor tissue removed from a 68-year-old Caucasian male during segmental lung resection. Pathology indicated invasive grade 3 squamous cell carcinoma and a metastatic tumor. Patient history included type II diabetes, thyroid disorder, depressive disorder, hyperlipidemia, esophageal ulcer, and tobacco use.  |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 226                          | 2755786  | THPIAZS08 | This subtracted THP-1 promonocyte cell line library was constructed using 5.76 million clones from a 5-aza-2'-deoxycytidine (AZ) treated THP-1 cell library. Starting RNA was made from THP-1 promonocyte cells treated for three days with 0.8 micromolar AZ. The hybridization probe for subtraction was derived from a similarly constructed library, made from RNA isolated from untreated THP-1 cells. 5.76 million clones from the AZ-treated THP-1 cell library were then subjected to two rounds of subtractive hybridization with 5 million clones from the untreated THP-1 cell library. Subtractive hybridization conditions were based on the methodologies of Swaroop et al., NAR (1991) 19:1954, and Bonaldo et al., Genome Research (1996) 6:791. THP-1 (ATCC TIB 202) is a human promonocyte line derived from peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia. |
| 227                          | 2831245  | TLYMN0T03 | The library was constructed using RNA isolated from nonactivated Th1 cells. These cells were differentiated from umbilical cord CD4 T cells with IL-12 and B7-transfected COS cells.  |
| 228                          | 3116250  | LUNGTUT13 | The library was constructed using RNA isolated from tumorous lung tissue removed from the right upper lobe of a 47-year-old Caucasian male during a segmental lung resection. Pathology indicated invasive grade 3 (of 4) adenocarcinoma. Family history included atherosclerotic coronary artery disease, and type II diabetes.  |
| 229                          | 3129630  | LUNGTUT12 | The library was constructed using RNA isolated from tumorous lung tissue removed from a 70-year-old Caucasian female during a lung lobectomy of the left upper lobe. Pathology indicated grade 3 (of 4) adenocarcinoma and vascular invasion. Patient history included tobacco abuse, depressive disorder, anxiety state, and skin cancer. Family history included cerebrovascular disease, congestive heart failure, colon cancer, depressive disorder, and primary liver.   |
| 230                          | 007632   | HMCIN0T01 | The library was constructed using RNA isolated from the HMC-1 human mast cell line derived from a 52-year-old female. Patient history included mast cell leukemia.  |
| 231                          | 1236968  | LUNGFET03 | The library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus who died at 20 weeks' gestation.  |
| 232                          | 1334153  | COLNNOT13 | The library was constructed using RNA isolated from ascending colon tissue of a 28-year-old Caucasian male with moderate chronic ulcerative colitis.  |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 233                          | 1396975  | BRAITUT08 | The library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe of a 47-year-old Caucasian male during excision of cerebral meningioma. Pathology indicated grade 4 fibrillary astrocytoma with focal tumoral radionecrosis. Patient history included cerebrovascular disease, deficiency anemia, hyperlipidemia, epilepsy, and tobacco use. Family history included cerebrovascular disease and malignant prostate neoplasm.                  |
| 234                          | 1501749  | SINTBST01 | The library was constructed using RNA isolated from ileum tissue removed from an 18-year-old Caucasian female during bowel anastomosis. Pathology indicated Crohn's disease of the ileum. Family history included cerebrovascular disease and atherosclerotic coronary artery disease.   |
| 235                          | 1575240  | LNODNOT03 | The library was constructed using RNA isolated from lymph node tissue removed from a 67-year-old Caucasian male during a segmental lung resection and bronchoscopy. This tissue was extensively necrotic with 10% viable tumor. Pathology for the associated tumor tissue indicated invasive grade 3-4 squamous cell carcinoma. Patient history included hemangioma. Family history included atherosclerotic coronary artery disease, benign hypertension, and congestive heart failure. |
| 236                          | 1647884  | PROSTUT09 | The library was constructed using RNA isolated from prostate tumor tissue removed from a 66-year-old Caucasian male during a radical prostatectomy, radical cystectomy, and urinary diversion. Pathology indicated grade 3 transitional cell carcinoma. Patient history included lung neoplasm, and benign hypertension. Family history included malignant breast neoplasm, tuberculosis, cerebrovascular disease, atherosclerotic coronary artery disease, and lung cancer.             |
| 237                          | 1661144  | BRSTNOT09 | The library was constructed using RNA isolated from breast tissue removed from a 45-year-old Caucasian female during unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated invasive nuclear grade 2-3 adenocarcinoma. Patient history included valvuloplasty of mitral valve and rheumatic heart disease. Family history included cardiovascular disease and type II diabetes.  |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 238                          | 1685409  | PROSNOT15 | The library was constructed using RNA isolated from diseased prostate tissue removed from a 66-year-old Caucasian male during radical prostatectomy and regional lymph node excision. Pathology indicated adenofibromatous hyperplasia. Pathology for the associated tumor tissue indicated adenocarcinoma (Gleason grade 2+3). The patient presented with elevated prostate specific antigen (PSA). Family history included prostate cancer, secondary bone cancer, and benign hypertension.  |
| 239                          | 1731419  | BRSTTUT08 | The library was constructed using RNA isolated from breast tumor tissue removed from a 45-year-old Caucasian female during unilateral extended simple mastectomy. Pathology indicated invasive nuclear grade 2-3 adenocarcinoma. Patient history included valvuloplasty of mitral valve and rheumatic heart disease. Family history included cardiovascular disease and type II diabetes.  |
| 240                          | 2650265  | BRSTNOT14 | The library was constructed using RNA isolated from breast tissue removed from a 62-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology for the associated tumor tissue indicated an invasive grade 3 (of 4), nuclear grade 3 (of 3) adenocarcinoma. Patient history included a benign colon neoplasm, hyperlipidemia, cardiac dysrhythmia, and obesity. Family history included cardiovascular and cerebrovascular disease and colon, ovary and lung cancer.  |
| 241                          | 2677129  | KIDNNOT19 | The library was constructed using RNA isolated from kidney tissue removed a 65-year-old Caucasian male during an exploratory laparotomy and nephroureterectomy. Pathology for the associated tumor tissue indicated grade 1 renal cell carcinoma within the upper pole of the left kidney. Patient history included malignant melanoma of the abdominal skin, benign neoplasm of colon, cerebrovascular disease, and umbilical hernia. Family history included myocardial infarction, atherosclerotic coronary artery disease, cerebrovascular disease, and prostate cancer. |
| 242                          | 3151073  | ADRENON04 | The normalized adrenal gland library was constructed from 1.36 x 1e6 independent clones from an adrenal tissue library. Starting RNA was made from adrenal gland tissue removed from a 20-year-old Caucasian male who died from head trauma. The library was normalized in two rounds using conditions adapted from Soares et al. (PNAS (1994) 91:9228-9232) and Bonaldo et al. (Genome Res (1996) 6: 791-806) using a significantly longer (48-hours/round) reannealing hybridization period.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 243                          | 3170095  | BRSTNOT18 | The library was constructed using RNA isolated from diseased breast tissue removed from a 57-year-old Caucasian female during a unilateral simple extended mastectomy. Pathology indicated mildly proliferative breast disease. Patient history included breast cancer and osteoarthritis. Family history included type II diabetes, gallbladder and breast cancer, and chronic lymphocytic leukemia.  |
| 244                          | 3475168  | LUNGNOT27 | The library was constructed using RNA isolated from lung tissue removed from a 17-year-old Hispanic female.  |
| 245                          | 3836893  | DENDTN01  | The library was constructed using RNA isolated from treated dendritic cells from peripheral blood.   |
| 246                          | 4072159  | KIDNNOT26 | The library was constructed using RNA isolated from left kidney medulla and cortex tissue removed from a 53-year-old Caucasian female during a nephroureterectomy. Pathology for the associated tumor tissue indicated grade 2 renal cell carcinoma involving the lower pole of the kidney. Patient history included hyperlipidemia, cardiac dysrhythmia, menorrhagia, cerebrovascular disease, atherosclerotic coronary artery disease, and tobacco abuse. Family history included cerebrovascular disease and atherosclerotic coronary artery disease. |
| 247                          | 1003916  | BRSTNOT03 | The library was constructed using RNA isolated from diseased breast tissue removed from a 54-year-old Caucasian female during a bilateral radical mastectomy. Pathology for the associated tumor tissue indicated residual invasive grade 3 mammary ductal adenocarcinoma. Patient history included kidney infection and condyloma acuminatum. Family history included benign hypertension, hyperlipidemia and a malignant neoplasm of the colon.  |
| 248                          | 2093492  | PANCNOT04 | The library was constructed using RNA isolated from the pancreatic tissue of a 5-year-old Caucasian male who died in a motor vehicle accident.   |
| 249                          | 2108789  | BRAITUT03 | The library was constructed using RNA isolated from brain tumor tissue removed from the left frontal lobe of a 17-year-old Caucasian female during excision of a cerebral meningeal lesion. Pathology indicated a grade 4 fibrillary giant and small-cell astrocytoma. Family history included benign hypertension and cerebrovascular disease.  |
| 250                          | 2171401  | ENDCN03   | The library was constructed using RNA isolated from dermal microvascular endothelial cells removed from a neonatal Caucasian male.   |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library    | Library Description   |
|------------------------------|----------|------------|---|
| 251                          | 2212530  | SINTFET03  | The library was constructed using RNA isolated from small intestine tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.  |
| 252                          | 2253036  | OVARTUT01  | The library was constructed using RNA isolated from ovarian tumor tissue removed from a 43-year-old Caucasian female during removal of the fallopian tubes and ovaries. Pathology indicated grade 2 mucinous cystadenocarcinoma involving the entire left ovary. Patient history included mitral valve disorder, pneumonia, and viral hepatitis. Family history included atherosclerotic coronary artery disease, pancreatic cancer, stress reaction, cerebrovascular disease, breast cancer, and uterine cancer. |
| 253                          | 2280161  | PROSNON01  | The normalized prostate library was constructed from 4.4 M independent clones from the PROSNOT11 library. Starting RNA was made from prostate tissue removed from a 28-year-old Caucasian male who died from a self-inflicted gunshot wound. The normalization and hybridization conditions were adapted from Soares, M.B. et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228-9232, using a longer (19 hour) reannealing hybridization period.  |
| 254                          | 2287485  | BRAINON01  | The library was constructed and normalized from 4.88 million independent clones from the BRAINOT03 library. RNA was made from brain tissue removed from a 26-year-old Caucasian male during cranioplasty and excision of a cerebral meningeal lesion. Pathology for the associated tumor tissue indicated a grade 4 oligoastrocytoma in the right fronto-parietal part of the brain.  |
| 255                          | 2380344  | ISL.TNOT01 | The library was constructed using RNA isolated from a pooled collection of pancreatic islet cells.  |
| 256                          | 2383171  | ISL.TNOT01 | The library was constructed using RNA isolated from a pooled collection of pancreatic islet cells.  |
| 257                          | 2396046  | THP1AZT01  | The library was constructed using RNA isolated from THP-1 promonocyte cells treated for three days with 0.8 micromolar 5-aza-2'-deoxycytidine. THP-1 (ATCC TIB 202) is a human promonocyte line derived from peripheral blood of a 1-year-old Caucasian male with acute monocytic leukemia.   |
| 258                          | 2456587  | ENDANOT01  | The library was constructed using RNA isolated from aortic endothelial cell tissue from an explanted heart removed from a male during a heart transplant.   |



TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description   |
|------------------------------|----------|-----------|---|
| 259                          | 2484813  | BONRTUT01 | The library was constructed using RNA isolated from rib tumor tissue removed from a 16-year-old Caucasian male during a rib osteotomy and a wedge resection of the lung. Pathology indicated a metastatic grade 3 (of 4) osteosarcoma, forming a mass involving the chest wall.   |
| 260                          | 2493851  | ADRETUT05 | The library was constructed RNA isolated from adrenal tumor tissue removed from a 52-year-old Caucasian female during a unilateral adrenalectomy. Pathology indicated a pheochromocytoma.   |
| 261                          | 2495719  | ADRETUT05 | The library was constructed RNA isolated from adrenal tumor tissue removed from a 52-year-old Caucasian female during a unilateral adrenalectomy. Pathology indicated a pheochromocytoma.   |
| 262                          | 2614153  | GBLANOT01 | The library was constructed using RNA isolated from diseased gallbladder tissue removed from a 53-year-old Caucasian female during a cholecystectomy. Pathology indicated mild chronic cholecystitis and cholelithiasis with approximately 150 mixed gallstones. Family history included benign hypertension.   |
| 263                          | 2655184  | THYMNOT04 | The library was constructed using RNA isolated from thymus tissue removed from a 3-year-old Caucasian male, who died from anoxia. Serologies were negative. The patient was not taking any medications.   |
| 264                          | 2848362  | BRSTTUT13 | The library was constructed using RNA isolated from breast tumor tissue removed from the right breast of a 46-year-old Caucasian female during a unilateral extended simple mastectomy with breast reconstruction. Pathology indicated an invasive grade 3 adenocarcinoma, ductal type with apocrine features and greater than 50% intraductal component. Patient history included breast cancer. |
| 265                          | 2849906  | BRSTTUT13 | The library was constructed using RNA isolated from breast tumor tissue removed from the right breast of a 46-year-old Caucasian female during a unilateral extended simple mastectomy with breast reconstruction. Pathology indicated an invasive grade 3 adenocarcinoma, ductal type with apocrine features and greater than 50% intraductal component. Patient history included breast cancer. |

TABLE 4 (cont.)

| Polynucleotide<br>SEQ ID NO: | Clone ID | Library   | Library Description  |
|------------------------------|----------|-----------|--|
| 266                          | 2899137  | DRGCNOT01 | The library was constructed using RNA isolated from dorsal root ganglion tissue removed from the cervical spine of a 32-year-old Caucasian male who died from acute pulmonary edema and bronchopneumonia, bilateral pleural and pericardial effusions, and malignant lymphoma (natural killer cell type). Patient history included probable cytomegalovirus, infection, hepatic congestion and steatosis, splenomegaly, hemorrhagic cystitis, thyroid hemorrhage, and Bell's palsy. Surgeries included colonoscopy, large intestine biopsy, adenotonsillectomy, and nasopharyngeal endoscopy and biopsy; treatment included radiation therapy. |
| 267                          | 2986229  | CARGDIT01 | The library was constructed using RNA isolated from diseased cartilage tissue. Patient history included osteoarthritis.  |
| 268                          | 3222081  | COLNNON03 | The normalized colon library was constructed from $2.84 \times 10^6$ independent clones from the COLNNOT07 library. Starting RNA was made from colon tissue removed from a 60-year-old Caucasian male during a left hemicolectomy. The normalization and hybridization conditions were adapted from Soares et al. (PNAS (1994) 91:9228-9232), Swaroop et al. (Nucl. Acids Res. (1991) 19:1954) and Bonaldo et al. (Genome Res (1996) 6: 791-806), using a significantly longer (48 hour) reannealing hybridization period.   |

Table 5

| Program           | Description   | Reference   | Parameter Threshold  |
|-------------------|---|---|--|
| ABI FACTURA       | A program that removes vector sequences and masks ambiguous bases in nucleic acid sequences.  | Perkin-Elmer Applied Biosystems, Foster City, CA.   |  |
| ABI/PARACEL FDF   | A Fast Data Finder useful in comparing and annotating amino acid or nucleic acid sequences.   | Perkin-Elmer Applied Biosystems, Foster City, CA; Paracel Inc., Pasadena, CA.   | Mismatch <50%  |
| ABI AutoAssembler | A program that assembles nucleic acid sequences.  | Perkin-Elmer Applied Biosystems, Foster City, CA.   |  |
| BLAST             | A Basic Local Alignment Search Tool useful in sequence similarity search for amino acid and nucleic acid sequences. BLAST includes five functions: blastp, blastn, blastx, tblastn, and tblastx.                    | Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410; Altschul, S.F. et al. (1997) Nucleic Acids Res. 25: 3389-3402.  | ESTs: Probability value= 1.0E-8 or less<br>Full Length sequences:<br>Probability value= 1.0E-10 or less  |
| FASTA             | A Pearson and Lipman algorithm that searches for similarity between a query sequence and a group of sequences of the same type. FASTA comprises at least five functions: fasta, tfasta, fastx, tfastx, and ssearch. | Pearson, W.R. and D.J. Lipman (1988) Proc. Natl. Acad. Sci. 85:2444-2448; Pearson, W.R. (1990) Methods Enzymol. 183: 63-98; and Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489.           | ESTs: fasta E value= 1.06E-6<br>Assembled ESTs: fasta Identity = 95% or greater and Match length=200 bases or greater; fastx E value= 1.0E-8 or less<br>Full Length sequences: fastx score= 100 or greater |
| BLIMPS            | A BLocks IMProved Searcher that matches a sequence against those in BLOCKS and PRINTS databases to search for gene families, sequence homology, and structural fingerprint regions.                                 | Henikoff, S and J.G. Henikoff, Nucl. Acid Res., 19:6565-72, 1991. J.G. Henikoff and S. Henikoff (1996) Methods Enzymol. 266:88-105; and Attwood, T.K. et al. (1997) J. Chem. Inf. Comput. Sci. 37: 417-424. | Score= 1000 or greater; Ratio of Score/Strength = 0.75 or larger; and Probability value= 1.0E-3 or less  |
| PFAM              | A Hidden Markov Models-based application useful for protein family search.  | Krogh, A. et al. (1994) J. Mol. Biol., 235:1501-1531; Sonnhammer, E.L.L. et al. (1988) Nucleic Acids Res. 26:320-322.   | Score= 10-50 bits, depending on individual protein families  |

Table 5 (cont.)

| Program     | Description   | Reference  | Parameter Threshold                                |
|-------------|---|--|--|
| ProfileScan | An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.   | Gribskov, M. et al. (1988) CABIOS 4:61-66;<br>Gribskov, et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25: 217-221.                            | Score= 4.0 or greater                              |
| Phred       | A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.  | Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.  |  |
| Phrap       | A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences. | Smith, T.F. and M. S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M. S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA. | Score= 120 or greater; Match length= 56 or greater |
| Consed      | A graphical tool for viewing and editing Phrap assemblies   | Gordon, D. et al. (1998) Genome Res. 8:195-202.  |  |
| SPScan      | A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.  | Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12: 431-439.   | Score=5 or greater                                 |
| Motifs      | A program that searches amino acid sequences for patterns that matched those defined in Prosite.  | Bairoch et al. <u>supra</u> ; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.  |  |

TABLE 6

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 135                      | 443531   | 443531H1                 | 1                                  | 253                              |
|                          |          | 1406807F6                | 152                                | 336                              |
|                          |          | 443531T6                 | 847                                | 355                              |
|                          |          | SBBA00451F1              | 396                                | 856                              |
|                          |          | SBBA00676F1              | 546                                | 865                              |
| 136                      | 632860   | 632860H1                 | 13                                 | 253                              |
|                          |          | 784715R3                 | 17                                 | 666                              |
|                          |          | 509590H1                 | 455                                | 706                              |
| 137                      | 670010   | 670010H1                 | 1                                  | 263                              |
|                          |          | 669971R1                 | 1                                  | 633                              |
| 138                      | 726498   | 726498H1                 | 13                                 | 263                              |
|                          |          | 726498R6                 | 13                                 | 489                              |
|                          |          | 866599R3                 | 7                                  | 660                              |
| 139                      | 795064   | 795064H1                 | 86                                 | 323                              |
|                          |          | 4339458H1                | 4                                  | 284                              |
|                          |          | 937605R3                 | 86                                 | 505                              |
|                          |          | 2381151F6                | 592                                | 1057                             |
|                          |          | 1466346F6                | 857                                | 1241                             |
| 140                      | 924925   | 924925H1                 | 111                                | 412                              |
|                          |          | 3268330H1                | 2                                  | 239                              |
|                          |          | 759120R3                 | 111                                | 629                              |
| 141                      | 962390   | 1907958F6                | 1                                  | 478                              |
|                          |          | 023569F1                 | 1122                               | 470                              |
|                          |          | 167282F1                 | 1216                               | 543                              |
|                          |          | 1309211F1                | 911                                | 1224                             |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO         | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|----------------------------------|------------------------------------|----------------------------------|
| 142                      | 1259405  | 1259405H1                        | 46                                 | 277                              |
|                          |          | 2472425H1                        | 331                                | 354                              |
|                          |          | 774303R1                         | 190                                | 743                              |
|                          |          | 1520779F1                        | 418                                | 1001                             |
|                          |          | 1693833F6                        | 914                                | 1467                             |
|                          |          | 1831858T6.comp<br>1527737T6.comp | 1336<br>1386                       | 1742<br>1829                     |
| 143                      | 1297384  | 1297384H1                        | 402                                | 641                              |
|                          |          | 1269310F6                        | 1                                  | 492                              |
|                          |          | 1457367F1                        | 792                                | 1380                             |
|                          |          | 415587R1                         | 1358                               | 1712                             |
|                          |          | SANA02967F1                      | 1143                               | 614                              |
| 144                      | 1299627  | 1299627H1                        | 1                                  | 250                              |
|                          |          | 1359140F6                        | 1004                               | 1573                             |
|                          |          | 1349224F1                        | 1330                               | 1731                             |
|                          |          | SBAA01431F1                      | 46                                 | 397                              |
|                          |          | SBAA02909F1                      | 868                                | 262                              |
|                          |          | SBAA01156F1                      | 901                                | 1266                             |
| 145                      | 1306026  | 1306026H1                        | 1                                  | 223                              |
|                          |          | 1464088R6                        | 302                                | 829                              |
|                          |          | SBAA02496F1                      | 92                                 | 568                              |
|                          |          | SBAA04305F1                      | 366                                | 883                              |
| 146                      | 1316219  | 1316219H1                        | 246                                | 491                              |
|                          |          | 2458603F6                        | 1                                  | 402                              |
|                          |          | 2504756T6                        | 980                                | 380                              |
| 147                      | 1329031  | 1329031H1                        | 1                                  | 264                              |
|                          |          | 1329031T6                        | 505                                | 1                                |
|                          |          | 1329031F6                        | 1                                  | 523                              |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 148                      | 1483050  | 1483050H1                | 722                                | 931                              |
|                          |          | 855049H1                 | 1                                  | 267                              |
|                          |          | 077017F1                 | 1069                               | 679                              |
|                          |          | 1483050F6                | 722                                | 1215                             |
|                          |          | 1480024T6                | 2063                               | 1315                             |
| 149                      | 1514160  | 1483050T6                | 2068                               | 1535                             |
|                          |          | 759486R1                 | 1762                               | 2089                             |
|                          |          | 1514160H1                | 1640                               | 1838                             |
|                          |          | 1866765T7                | 2383                               | 2210                             |
|                          |          | 782676R1                 | 1652                               | 1875                             |
| 150                      | 1603403  | 008055X4                 | 1090                               | 1804                             |
|                          |          | 008055X5                 | 1316                               | 1952                             |
|                          |          | 1866765F6                | 2209                               | 2391                             |
|                          |          | SAOA03127F1              | 2129                               | 1703                             |
|                          |          | 1603403H1                | 7                                  | 224                              |
| 151                      | 1652303  | 372910F1                 | 420                                | 44                               |
|                          |          | 733299R7                 | 219                                | 420                              |
|                          |          | 1652303H1                | 4                                  | 256                              |
|                          |          | 1671806H1                | 1                                  | 224                              |
|                          |          | 1341743T1                | 2069                               | 1900                             |
| 151                      | 1652303  | 3803812H1                | 389                                | 697                              |
|                          |          | 1878546F6                | 747                                | 1344                             |
|                          |          | 1428640F1                | 1081                               | 1664                             |
|                          |          | 2058609R6                | 1715                               | 2098                             |
|                          |          | 1331621F1                | 1780                               | 2096                             |
|                          |          | 1306331T1                | 1897                               | 2098                             |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 152                      | 1693358  | 1693358H1                | 41                                 | 125                              |
|                          |          | 2498265H1                | 1                                  | 252                              |
|                          |          | 1867125F6                | 205                                | 373                              |
|                          |          | 1693358T6                | 1094                               | 416                              |
|                          |          | 2245848R6                | 737                                | 1103                             |
| 153                      | 1707711  | 1707711H1                | 408                                | 626                              |
|                          |          | 1484609T1                | 2165                               | 1855                             |
|                          |          | 1707711F6                | 408                                | 987                              |
|                          |          | 1267959F1                | 1721                               | 2182                             |
|                          |          | 1484609F1                | 1855                               | 2178                             |
|                          |          | SAJA00930F1              | 544                                | 1132                             |
|                          |          | SAJA01300R1              | 1675                               | 1212                             |
|                          |          | SAJA00999R1              | 1675                               | 1142                             |
| 154                      | 1738735  | 1738735H1                | 7                                  | 236                              |
|                          |          | SAJA00944R1              | 393                                | 5                                |
|                          |          | SAJA00137F1              | 913                                | 685                              |
|                          |          | SAJA03629F1              | 435                                | 42                               |
| 155                      | 1749147  | 1749147H1                | 1                                  | 276                              |
| 155                      |          | 1749147F6                | 47                                 | 457                              |
| 155                      |          | 1749147T6                | 479                                | 1                                |
| 156                      | 1817722  | 1817722H1                | 1                                  | 268                              |
|                          |          | 2011085H1                | 344                                | 545                              |
| 157                      | 1831290  | 1831290H1                | 10                                 | 257                              |
|                          |          | 3473958H1                | 70                                 | 242                              |
|                          |          | 1972268F6                | 163                                | 617                              |
|                          |          | 1301277F1                | 413                                | 852                              |
|                          |          | 1521574F1                | 1024                               | 1602                             |
|                          |          | 1561690T6                | 1729                               | 1058                             |
|                          |          | 891461R1                 | 1261                               | 1738                             |



TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 158                      | 1831477  | 1831477H1                | 59                                 | 337                              |
|                          |          | 1582867H1                | 1                                  | 199                              |
|                          |          | 1336769T1                | 1986                               | 1639                             |
|                          |          | 1933092H1                | 525                                | 789                              |
|                          |          | 1519909F1                | 841                                | 1296                             |
|                          |          | 1220946H1                | 1061                               | 1318                             |
|                          |          | 809556T1                 | 1983                               | 1687                             |
|                          |          | 1217559T1                | 2002                               | 1445                             |
|                          |          | 1309225F1                | 1747                               | 2001                             |
| 159                      | 1841607  | 1841607H1                | 13                                 | 192                              |
|                          |          | SBHA03588F1              | 13                                 | 172                              |
| 160                      | 1852391  | 1852391H1                | 98                                 | 367                              |
|                          |          | 734140H1                 | 1                                  | 225                              |
|                          |          | 1852391F6                | 98                                 | 542                              |
| 161                      | 1854555  | 1854555H1                | 1                                  | 265                              |
|                          |          | 2511711H1                | 37                                 | 58                               |
|                          |          | 782453R1                 | 223                                | 712                              |
|                          |          | 1854555F6                | 1                                  | 346                              |
|                          |          | 1840675T6                | 1046                               | 860                              |
|                          |          | 2109736H1                | 938                                | 1054                             |
|                          |          | 1855755H1                | 17                                 | 224                              |
| 162                      | 1855755  | 3040236H1                | 1                                  | 179                              |
|                          |          | 1283207F1                | 306                                | 816                              |
|                          |          | 833763T1                 | 1148                               | 835                              |
|                          |          | 1920926R6                | 854                                | 1161                             |
| 163                      | 1861434  | 1861434H1                | 13                                 | 253                              |
|                          |          | 1861434T6                | 872                                | 261                              |
|                          |          | SARA01525F1              | 426                                | 808                              |
|                          |          | SARA02548F1              | 587                                | 889                              |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO.: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|---------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 164                       | 1872334  | 1872334H1                | 1                                  | 229                              |
|                           |          | 1872334F6                | 1                                  | 424                              |
|                           |          | SBGA03684F1              | 358                                | 425                              |
| 165                       | 1877230  | 1877230H1                | 1405                               | 1677                             |
|                           |          | 2519841H1                | 1                                  | 251                              |
|                           |          | 1877230T6                | 1903                               | 1405                             |
|                           |          | 1254693F1                | 335                                | 716                              |
|                           |          | 077020R1                 | 682                                | 1414                             |
|                           |          | 1232336F1                | 906                                | 1507                             |
|                           |          | 1004952R6                | 1451                               | 1904                             |
|                           |          | SARA01879F1              | 1545                               | 1921                             |
|                           |          | SARA02654F1              | 1545                               | 1923                             |
|                           |          |                          |                                    |                                  |
| 166                       | 1877885  | 1877885H1                | 68                                 | 323                              |
|                           |          | 508020F1                 | 499                                | 51                               |
|                           |          | 2751126R6                | 219                                | 516                              |
|                           |          | SARA02571F1              | 407                                | 499                              |
| 167                       | 1889269  | 1889269H1                | 757                                | 1020                             |
|                           |          | 1915551H1                | 1                                  | 191                              |
|                           |          | 629493X12                | 481                                | 865                              |
|                           |          | 1441289F1                | 693                                | 865                              |
|                           |          | 1215274X34F1             | 1106                               | 1631                             |
|                           |          | 1818447F6                | 1307                               | 1540                             |
|                           |          | 1208463R1                | 1372                               | 1493                             |
|                           |          |                          |                                    |                                  |
| 168                       | 1890243  | 1890243H1                | 9                                  | 268                              |
|                           |          | SARA01884F1              | 521                                | 168                              |
|                           |          | SATA00046F1              | 1057                               | 851                              |
|                           |          | SARA03294F1              | 1329                               | 910                              |
|                           |          | SARA02790F1              | 1138                               | 1535                             |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO   | Starting Nucleotide of<br>Fragment                    | Ending Nucleotide of<br>Fragment                          |
|--------------------------|----------|--|---|---|
| 169                      | 1900433  | 1900433H1<br>SATA00396F1<br>SATA02742F1  | 1<br>409<br>1   | 242<br>124<br>294   |
| 170                      | 1909441  | 1909441H1<br>1398811F1<br>3039939H1<br>3324740H1<br>1442131F6<br>2254056H1<br>2199453T6<br>1698531H1 | 786<br>1<br>607<br>685<br>787<br>1423<br>1955<br>1968 | 1048<br>550<br>876<br>944<br>1232<br>1522<br>1351<br>1796 |
| 171                      | 1932226  | 1932226H1<br>2320569H1<br>1932226F6<br>2469455T6<br>2469455F6<br>1907140F6<br>SATA02592F1            | 294<br>1<br>294<br>1475<br>1034<br>1158<br>857        | 510<br>266<br>685<br>1071<br>1492<br>1482<br>518          |
| 172                      | 1932647  | 1932647H1<br>1492745T1<br>1492745H1<br>SASA02355F1<br>SASA00117F1<br>SASA00192F1                     | 17<br>1582<br>1418<br>386<br>250<br>515               | 246<br>1418<br>1599<br>19<br>569<br>816                   |
| 173                      | 2124245  | 2124245H1<br>1235393F1<br>1402264F6<br>1303990F1<br>1402264T6  | 45<br>495<br>323<br>682<br>1613                       | 190<br>895<br>925<br>1240<br>950                          |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 174                      | 2132626  | 2132626H1                | 406                                | 651                              |
|                          |          | 1723432T6                | 1299                               | 746                              |
|                          |          | 2132626R6                | 406                                | 904                              |
|                          |          | 1736723T6                | 1292                               | 857                              |
| 175                      | 2280639  | 1504738F1                | 868                                | 1320                             |
|                          |          | 2280639H1                | 28                                 | 303                              |
| 176                      | 2292356  | 1377560F6                | 261                                | 777                              |
|                          |          | 2292356H1                | 717                                | 968                              |
|                          |          | 4086827H1                | 1                                  | 275                              |
|                          |          | 175442F6                 | 232                                | 577                              |
|                          |          | 3571126H1                | 497                                | 808                              |
| 177                      | 2349310  | 1601305F6                | 808                                | 1464                             |
|                          |          | 2349310H1                | 1                                  | 236                              |
| 178                      | 2373227  | 2349310T6                | 682                                | 2                                |
|                          |          | 2373227H1                | 298                                | 524                              |
|                          |          | 3316444H1                | 801                                | 1053                             |
|                          |          | 302685R6                 | 1141                               | 1496                             |
|                          |          | SASA02181F1              | 577                                | 1                                |
| 179                      | 2457682  | SASA01923F1              | 963                                | 466                              |
|                          |          | SASA03516F1              | 1102                               | 1249                             |
| 180                      | 2480426  | 2457682H1                | 1                                  | 226                              |
|                          |          | 2457682F6                | 1                                  | 554                              |
| 180                      | 2480426  | 2480426H1                | 1                                  | 213                              |
|                          |          | 2480426F6                | 1                                  | 501                              |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 181                      | 2503743  | 2503743H1                | 6                                  | 222                              |
|                          |          | 1853909H1                | 1                                  | 272                              |
|                          |          | 1517619F1                | 172                                | 830                              |
|                          |          | 1467896F6                | 540                                | 1112                             |
|                          |          | 490031F1                 | 1647                               | 1068                             |
|                          |          | 1208654R1                | 1382                               | 1633                             |
| 182                      | 2537684  | 880544R1                 | 1450                               | 1648                             |
|                          |          | 2537684H1                | 434                                | 682                              |
|                          |          | 2005493H1                | 1                                  | 194                              |
|                          |          | 730969H1                 | 307                                | 547                              |
|                          |          | 916487H1                 | 723                                | 989                              |
|                          |          | 996135R1                 | 997                                | 1598                             |
| 183                      | 2593853  | 1920738R6                | 1306                               | 1692                             |
|                          |          | 1957710F6                | 1472                               | 1692                             |
|                          |          | 2593853H1                | 1                                  | 252                              |
|                          |          | 807497H1                 | 2                                  | 217                              |
|                          |          | 914020R6                 | 284                                | 740                              |
|                          |          | 889992R1                 | 416                                | 729                              |
| 184                      | 2622354  | 2622354H1                | 3                                  | 266                              |
|                          |          | 2623992H1                | 1                                  | 246                              |
|                          |          | 1556510F6                | 81                                 | 258                              |
| 185                      | 2641377  | 2641377H1                | 126                                | 369                              |
|                          |          | 4341415H2                | 10                                 | 345                              |
|                          |          | SBCA07049F3              | 126                                | 599                              |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 186                      | 2674857  | 2674857H1                | 139                                | 393                              |
|                          |          | 1872373H1                | 1                                  | 270                              |
|                          |          | 470512R6                 | 1486                               | 1502                             |
|                          |          | 1728547H1                | 1285                               | 1508                             |
|                          |          | 3013651F6                | 1423                               | 1987                             |
|                          |          | SBCA01366F1              | 819                                | 385                              |
| 187                      | 2758485  | SBCA00694F1              | 973                                | 1198                             |
|                          |          | 2758485H1                | 20                                 | 267                              |
|                          |          | 3097533H1                | 1                                  | 158                              |
|                          |          | 1578959F6                | 291                                | 771                              |
|                          |          | 2763296H1                | 63                                 | 301                              |
|                          |          | 3486025F6                | 1                                  | 130                              |
| 188                      | 2763296  | SBDA07002F3              | 63                                 | 687                              |
|                          |          | 2779436H1                | 1                                  | 233                              |
|                          |          | 2779436F6                | 1                                  | 577                              |
|                          |          | SBDA07009F3              | 1                                  | 608                              |
|                          |          | 2808528H1                | 25                                 | 335                              |
|                          |          | 2611513F6                | 2                                  | 489                              |
| 190                      | 2808528  | SBDA07021T3              | 1058                               | 443                              |
|                          |          | 2809230H1                | 409                                | 630                              |
|                          |          | 2213849H1                | 1                                  | 133                              |
|                          |          | 711706R6                 | 396                                | 691                              |
|                          |          | 958323R1                 | 407                                | 800                              |
|                          |          | 030732F1                 | 1366                               | 623                              |
| 192                      | 2816821  | 2816821H1                | 210                                | 501                              |
|                          |          | 3746964H1                | 1                                  | 307                              |
|                          |          | 2816821F6                | 210                                | 682                              |
|                          |          | 948722T6                 | 959                                | 527                              |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 193                      | 2817268  | 2817268H1                | 42                                 | 282                              |
|                          |          | 3591308H1                | 13                                 | 264                              |
|                          |          | 419522R1                 | 179                                | 808                              |
|                          |          | 2073028F6                | 446                                | 924                              |
|                          |          | 1308781F6                | 869                                | 1112                             |
| 194                      | 2923165  | 2923165H1                | 8                                  | 295                              |
|                          |          | 2011630H1                | 18                                 | 238                              |
|                          |          | 1457250F1                | 268                                | 856                              |
|                          |          | 754668R1                 | 327                                | 878                              |
|                          |          | 1406510F6                | 558                                | 901                              |
| 195                      | 2949822  | 2949822H1                | 1                                  | 280                              |
|                          |          | SBD A07078F3             | 1                                  | 606                              |
| 196                      | 2992192  | 2992192H1                | 25                                 | 321                              |
|                          |          | 2534324H2                | 1                                  | 240                              |
|                          |          | 2815255T6                | 690                                | 219                              |
|                          |          | 1551107T6                | 893                                | 471                              |
|                          |          | 1551107R6                | 471                                | 690                              |
| 197                      | 2992458  | 2992458H1                | 48                                 | 362                              |
|                          |          | 2618951H1                | 1                                  | 247                              |
|                          |          | 1479252F1                | 163                                | 610                              |
|                          |          | 1879054H1                | 563                                | 840                              |
|                          |          | 1879054F6                | 563                                | 1096                             |
|                          |          | 2215240H1                | 951                                | 1202                             |
|                          |          | 1535968T1                | 1729                               | 1173                             |

TABLE 6 (cont.)

| Nucleotide<br>SEQ ID NO: | Clone ID | Fragment of<br>SEQ ID NO | Starting Nucleotide of<br>Fragment | Ending Nucleotide of<br>Fragment |
|--------------------------|----------|--------------------------|------------------------------------|----------------------------------|
| 198                      | 3044710  | 3044710H1                | 652                                | 952                              |
|                          |          | 3741773H1                | 1                                  | 283                              |
|                          |          | 859906X42C1              | 94                                 | 192                              |
|                          |          | 1534347F1                | 90                                 | 268                              |
|                          |          | 1421122F1                | 830                                | 1392                             |
|                          |          | 1303865F1                | 1033                               | 1487                             |
|                          |          | 1704452F6                | 1432                               | 1934                             |
|                          |          | 1251642F1                | 2006                               | 1544                             |
|                          |          | 1781694R6                | 1894                               | 2017                             |
| 199                      | 3120415  | 3120415H1                | 72                                 | 363                              |
|                          |          | 1360123T1                | 523                                | 141                              |
|                          |          | 1375015H1                | 380                                | 526                              |



What is claimed is:

1. A substantially purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134 (SEQ ID NO:1-134), and fragments thereof.

2. A substantially purified variant having at least 90% amino acid sequence identity to the amino acid sequence of claim 1.

3. An isolated and purified polynucleotide encoding the polypeptide of claim 1.
4. An isolated and purified polynucleotide variant having at least 90% polynucleotide sequence identity to the polynucleotide of claim 3.
- 5 5. An isolated and purified polynucleotide which hybridizes under stringent conditions to the polynucleotide of claim 3.
6. An isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide of claim 3.
7. A method for detecting a polynucleotide, the method comprising the steps  
10 of:
  - (a) hybridizing the polynucleotide of claim 6 to at least one nucleic acid in a sample, thereby forming a hybridization complex; and
  - (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of the polynucleotide in the  
15 sample.
8. The method of claim 7 further comprising amplifying the polynucleotide prior to hybridization.
9. An isolated and purified polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:135, SEQ ID NO:136, SEQ  
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- 15           10.    An isolated and purified polynucleotide variant having at least 90% polynucleotide sequence identity to the polynucleotide of claim 9.
11.    An isolated and purified polynucleotide having a sequence which is complementary to the polynucleotide of claim 9.
12.    An expression vector comprising at least a fragment of the polynucleotide  
20   of claim 3.
13.    A host cell comprising the expression vector of claim 12.
14.    A method for producing a polypeptide, the method comprising the steps of:
  - a)     culturing the host cell of claim 13 under conditions suitable for the expression of the polypeptide; and
  - 25       b)     recovering the polypeptide from the host cell culture.
15.    A pharmaceutical composition comprising the polypeptide of claim 1 in conjunction with a suitable pharmaceutical carrier.
16.    A purified antibody which specifically binds to the polypeptide of claim 1.
17.    A purified agonist of the polypeptide of claim 1.
- 30           18.    A purified antagonist of the polypeptide of claim 1.

19. A method for treating or preventing a disorder associated with decreased expression or activity of HSPP, the method comprising administering to a subject in need of such treatment an effective amount of the pharmaceutical composition of claim 15.

20. A method for treating or preventing a disorder associated with increased  
5 expression or activity of HSPP, the method comprising administering to a subject in need of such treatment an effective amount of the antagonist of claim 18.

## SEQUENCE LISTING

<110> INCYTE PHARMACEUTICALS, INC.  
 LAL, Preeti  
 TANG, Y. Tom  
 GORGONE, Gina A.  
 CORLEY, Neil C.  
 GUEGLER, Karl J.  
 BAUGHN, Mariah R.  
 AKERBLOM, Ingrid E.  
 AU-YOUNG, Janice  
 YUE, Henry  
 PATTERSON, Chandra  
 REDDY, Roopa  
 HILLMAN, Jennifer L.  
 BANDMAN, Olga

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 Trp Leu Glu Pro Arg Gln Leu Arg Trp Ser Trp Thr Glu Pro Pro  
                   35                  40                  45  
 Phe Thr Leu Leu Asp Ser Leu Gly Leu Arg Ala Ala Gln Asp Ser  
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 Cys Ser Phe Thr Thr Leu Val Pro Leu Thr Leu Asp Ser Ser Phe  
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 Met Thr Val Asn Val Val Pro Phe Val Trp Thr Ser Ser Phe Phe  
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 Thr Pro Leu Leu Ile Asp Gly Val Thr Arg Ile Gln Ala Thr Trp  
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 Phe Arg Cys Arg Val Ser Val Ala Arg Glu His Leu Pro Ser Arg  
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 Ser Cys Gln Pro Val Lys Gly His Gly Thr Leu Gly Glu Ser Pro  
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 35 40 45  
 His Gly Arg Gln Ala Arg Ala Cys Glu Asn Leu Arg Asn Gln Thr  
 50 55 60  
 Arg Val Ala Thr Lys Val Glu Pro Gln Lys Gly Arg Ser Thr Glu  
 65 70 75  
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 35 40 45  
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 50 55 60  
 Leu Ala Ile Val Pro Asn Val Arg Ile Ser Trp Arg Arg Gly His  
 65 70 75  
 Phe His Gly Gln Ser Phe Tyr Ser Thr Arg Pro Pro Ser Ile His  
 80 85 90  
 Lys Asp Tyr Val Asn Arg Leu Phe Leu Asn Trp Thr Glu Gly Gln  
 95 100 105  
 Glu Ser Gly Phe Leu Arg Ile Ser Asn Leu Arg Lys Glu Asp Gln  
 110 115 120  
 Ser Val Tyr Phe Cys Arg Val Glu Leu Asp Thr Arg Arg Ser Gly  
 125 130 135  
 Arg Gln Gln Leu Gln Ser Ile Lys Gly Thr Lys Leu Thr Ile Thr



|                 |   |  |     |  |     |
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|                 | 155   |  | 160 |  | 165 |
| Thr Ile Ala Gly | Leu Arg Val Thr Glu Ser Lys Gly His Ser Glu |  |     |  |     |
|                 | 170   |  | 175 |  | 180 |
| Ser Trp His Leu | Ser Leu Asp Thr Ala Ile Arg Val Ala Leu Ala |  |     |  |     |
|                 | 185   |  | 190 |  | 195 |
| Val Ala Val Leu | Lys Thr Val Ile Leu Gly Leu Leu Cys Leu Leu |  |     |  |     |
|                 | 200   |  | 205 |  | 210 |
| Leu Leu Trp Trp | Arg Arg Arg Lys Gly Ser Arg Ala Pro Ser Ser |  |     |  |     |
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| Ser Asp Ala Ala Lys Asn Phe Glu Asp Val Arg Cys Lys Cys Ile |     |         |
|   | 35  | 40 45   |
| Cys Pro Pro Tyr Lys Glu Asn Ser Gly His Ile Tyr Asn Lys Asn |     |         |
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| Ile Ser Gln Lys Asp Cys Asp Cys Leu His Val Val Glu Pro Met |     |         |
|   | 65  | 70 75   |
| Pro Val Arg Gly Pro Asp Val Glu Ala Tyr Cys Leu Arg Cys Glu |     |         |
|   | 80  | 85 90   |
| Cys Lys Tyr Glu Glu Arg Ser Ser Val Thr Ile Lys Val Thr Ile |     |         |
|   | 95  | 100 105 |
| Ile Ile Tyr Leu Ser Ile Leu Gly Leu Leu Leu Tyr Met Val     |     |         |
|   | 110 | 115 120 |
| Tyr Leu Thr Leu Val Glu Pro Ile Leu Lys Arg Arg Leu Phe Gly |     |         |
|   | 125 | 130 135 |
| His Ala Gln Leu Ile Gln Ser Asp Asp Asp Ile Gly Asp His Gln |     |         |
|   | 140 | 145 150 |
| Pro Phe Ala Asn Ala His Asp Val Leu Ala Arg Ser Arg Ser Arg |     |         |
|   | 155 | 160 165 |
| Ala Asn Val Leu Asn Lys Val Glu Tyr Ala Gln Gln Arg Trp Lys |     |         |
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| Val Leu Ser   |     |         |

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 Thr Ala Ile Ala Gly Ile Val Phe Gly Ile Val Phe Ile Met Gly  
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 Val Ile Ala Gly Ile Ala Ile Cys Ile Cys Met Cys Met Lys Asn  
                   80                  85                  90  
 His Arg Ala Thr Arg Val Gly Ile Leu Arg Thr Thr His Ile Asn  
                   95                  100                  105  
 Thr Val Ser Ser Tyr Pro Gly Pro Pro Pro Tyr Gly His Asp His  
                   110                  115                  120  
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 Asn Ala Arg Lys

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 35 40 45  
 Ser Val Pro Ser Gly Glu Pro Gly Arg Glu Lys Lys Ser Asn Ser  
 50 55 60  
 Pro Lys His Val Tyr Ser Ile Ala Ser Lys Gly Ser Lys Phe Lys  
 65 70 75  
 Glu Leu Val Thr His Gly Asp Ala Ser Thr Glu Asn Asp Val Leu  
 80 85 90  
 Thr Asn Pro Ile Ser Glu Glu Thr Thr Thr Phe Pro Thr Gly Gly  
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 Glu Glu Pro Tyr Ile Glu Asn Glu Glu Pro Glu Pro Glu Pro Glu  
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Gly Met Asp Thr Phe Ile Arg Val Leu Gln Lys Leu Asn Ser Ile
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His Arg Val Thr Thr Ile Ser Met Ala Arg Cys Thr Leu Thr Leu
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Gln Gly Val Asn Glu Lys Leu Thr Ile Ser Glu Glu Thr Leu Ala
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Leu Lys Val Pro Glu Gly Phe Phe Ser Gly Leu Ile Leu Leu Ser
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&lt;223&gt; Incyte Clone No: 1329031

&lt;400&gt; 13

```

Met Pro Ser Pro Gly Thr Val Cys Ser Leu Leu Leu Leu Gly Met
 1              5              10              15
Leu Trp Leu Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro
      20              25              30
Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro
      35              40              45
Ala Lys Leu Gln Pro Arg Ala Leu Ala Gly Trp Leu Arg Pro Glu
      50              55              60
Asp Gly Gly Gln Ala Glu Gly Ala Glu Asp Glu Leu Glu Val Arg
      65              70              75
Phe Asn Ala Pro Phe Asp Val Gly Ile Lys Leu Ser Gly Val Gln
      80              85              90
Tyr Gln Gln His Ser Gln Ala Leu Gly Lys Phe Leu Gln Asp Ile

```

|   |     |     |     |
|---|-----|-----|-----|
|   | 95  | 100 | 105 |
| Leu Trp Glu Glu Ala Lys Glu Ala Pro Ala Asp Lys |     |     |     |
|   | 110 | 115 |     |

<210> 14  
 <211> 253  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1483050

<400> 14  
 Met Asp Asn Arg Phe Ala Thr Ala Phe Val Ile Ala Cys Val Leu  
   1                  5                  10                  15  
 Ser Leu Ile Ser Thr Ile Tyr Met Ala Ala Ser Ile Gly Thr Asp  
                   20                  25                  30  
 Phe Trp Tyr Glu Tyr Arg Ser Pro Val Gln Glu Asn Ser Ser Asp  
                   35                  40                  45  
 Leu Asn Lys Ser Ile Trp Asp Glu Phe Ile Ser Asp Glu Ala Asp  
                   50                  55                  60  
 Glu Lys Thr Tyr Asn Asp Ala Leu Phe Arg Tyr Asn Gly Thr Val  
                   65                  70                  75  
 Gly Leu Trp Arg Arg Cys Ile Thr Ile Pro Lys Asn Met His Trp  
                   80                  85                  90  
 Tyr Ser Pro Pro Glu Arg Thr Glu Ser Phe Asp Val Val Thr Lys  
                   95                  100                 105  
 Cys Val Ser Phe Thr Leu Thr Glu Gln Phe Met Glu Lys Phe Val  
                  110                 115                 120  
 Asp Pro Gly Asn His Asn Ser Gly Ile Asp Leu Leu Arg Thr Tyr  
                  125                 130                 135  
 Leu Trp Arg Cys Gln Phe Leu Leu Pro Phe Val Ser Leu Gly Leu  
                  140                 145                 150  
 Met Cys Phe Gly Ala Leu Ile Gly Leu Cys Ala Cys Ile Cys Arg  
                  155                 160                 165  
 Ser Leu Tyr Pro Thr Ile Ala Thr Gly Ile Leu His Leu Leu Ala  
                  170                 175                 180  
 Gly Leu Cys Thr Leu Gly Ser Val Ser Cys Tyr Val Ala Gly Ile  
                  185                 190                 195  
 Glu Leu Leu His Gln Lys Leu Glu Leu Pro Asp Asn Val Ser Gly  
                  200                 205                 210  
 Glu Phe Gly Trp Ser Phe Cys Leu Ala Cys Val Ser Ala Pro Leu  
                  215                 220                 225  
 Gln Phe Met Ala Ser Ala Leu Phe Ile Trp Ala Ala His Thr Asn  
                  230                 235                 240  
 Arg Lys Glu Tyr Thr Leu Met Lys Ala Tyr Arg Val Ala  
                  245                 250

<210> 15  
 <211> 171

<212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1514160

<400> 15  
 Met Ser Leu Pro Ile Pro Trp Leu Ser Leu Pro Pro Cys Pro Ile  
     1                    5                    10                    15  
 Leu Gly Gln Pro Ala Gly Leu Leu Leu Trp Leu Phe Arg Pro Phe  
                     20                    25                    30  
 Ser Gln Cys Cys Gln Cys Pro Trp Glu Gly Arg Ala Ser Leu Arg  
                     35                    40                    45  
 His Pro Asn Gly Pro Ser Gly Cys Arg Glu Ala Glu Ala Trp Pro  
                     50                    55                    60  
 Gln Arg Ser Leu Leu Arg Gln Gln Leu Gln Gln Ala His Pro Leu  
                     65                    70                    75  
 Pro Thr Leu Pro Thr Pro Glu Arg Leu Pro Glu Gln Met Leu Phe  
                     80                    85                    90  
 Pro Ser Ser Ser Ser Lys Pro Phe Ser Leu Leu Ser Leu Thr Ile  
                     95                    100                    105  
 Trp Ala Arg Leu Val Gly Arg Leu Thr Asn Arg Ile Cys Pro Val  
                     110                    115                    120  
 Pro Pro Gly Ser Val Ala Ser Ser Met Ser Leu Gln Ala Gly Arg  
                     125                    130                    135  
 Cys Gly Asn Pro Val Val Leu Pro Gln Pro Met Pro Pro Gly Leu  
                     140                    145                    150  
 Leu Cys Met Asn Glu Cys Ser Leu Val Pro Gly Leu Gly Arg Gly  
                     155                    160                    165  
 Gln Val Asn Ser Arg Val  
                     170

<210> 16  
 <211> 78  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1603403

<400> 16  
 Met Gly Ser Gly Leu Pro Leu Val Leu Leu Leu Thr Leu Leu Gly  
     1                    5                    10                    15  
 Ser Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu Lys Leu  
                     20                    25                    30  
 Lys Glu Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe Leu  
                     35                    40                    45  
 Glu Leu Leu Glu Lys Leu Cys Leu Leu Leu His Leu Pro Ser Gly  
                     50                    55                    60  
 Thr Ser Val Thr Leu His His Ala Arg Ser Gln His His Val Val  
                     65                    70                    75  
 Cys Asn Thr

<210> 17  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1652303

<400> 17  
 Met Lys Leu Leu Ser Cys Leu Leu Phe Leu Lys Ala Pro Leu Tyr  
   1                  5                  10                  15  
 Pro Thr Leu Cys Ser Lys Asp Pro Arg Ala Gly His Ser Leu Ile  
                   20                  25                  30  
 Cys Gly Gln Ala Gly Gln Ile Pro Glu Ala Gln Leu Gly Phe Ser  
                   35                  40                  45  
 Ser Asp Phe Lys Leu Cys Trp Cys Trp Asp Gln Gln Lys Ala Asn  
                   50                  55                  60  
 Val Gln Pro Thr His Arg Thr Val Arg Gly Leu  
                   65                  70

<210> 18  
 <211> 188  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1693358

<400> 18  
 Met Val Pro Gly Ala Ala Gly Trp Cys Cys Leu Val Leu Trp Leu  
   1                  5                  10                  15  
 Pro Ala Cys Val Ala Ala His Gly Phe Arg Ile His Asp Tyr Leu  
                   20                  25                  30  
 Tyr Phe Gln Val Leu Ser Pro Gly Asp Ile Arg Tyr Ile Phe Thr  
                   35                  40                  45  
 Ala Thr Pro Ala Lys Asp Phe Gly Gly Ile Phe His Thr Arg Tyr  
                   50                  55                  60  
 Glu Gln Ile His Leu Val Pro Ala Glu Pro Pro Glu Ala Cys Gly  
                   65                  70                  75  
 Glu Leu Ser Asn Gly Phe Phe Ile Gln Asp Gln Ile Ala Leu Val  
                   80                  85                  90  
 Glu Arg Gly Gly Cys Ser Phe Leu Ser Lys Thr Arg Val Val Gln  
                   95                  100                 105  
 Glu His Gly Gly Arg Ala Val Ile Ile Ser Asp Asn Ala Val Asp  
                  110                 115                 120  
 Asn Asp Ser Phe Tyr Val Glu Met Ile Gln Asp Ser Thr Gln Arg  
                  125                 130                 135  
 Thr Ala Asp Ile Pro Ala Leu Phe Leu Leu Gly Arg Asp Gly Tyr  
                  140                 145                 150

```

Met Ile Arg Arg Ser Leu Glu Gln His Gly Leu Pro Trp Ala Ile
      155      160      165
Ile Ser Ile Pro Val Asn Val Thr Ser Ile Pro Thr Phe Glu Leu
      170      175      180
Leu Gln Pro Pro Trp Thr Phe Trp
      185

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<210> 19
<211> 80
<212> PRT
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte Clone No: 1707711

```

```

<400> 19
Met Lys Ala Gln Pro Leu Glu Ala Leu Leu Leu Val Ala Leu Val
  1      5      10      15
Leu Ser Phe Cys Gly Val Trp Phe Glu Asp Trp Leu Ser Lys Trp
      20      25      30
Arg Phe Gln Cys Ile Phe Gln Leu Ala His Gln Pro Ala Leu Val
      35      40      45
Asn Ile Gln Phe Arg Gly Thr Val Leu Gly Ser Glu Thr Phe Leu
      50      55      60
Gly Ala Glu Glu Asn Ser Ala Asp Val Arg Ser Trp Gln Thr Leu
      65      70      75
Ser Tyr Phe Glu Leu
      80

```

```

<210> 20
<211> 80
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 1738735

```

```

<400> 20
Met Ile Asp Leu Trp Leu Pro Ala Leu Phe Val Leu Val Ala Leu
  1      5      10      15
Glu Ser Leu Leu Leu Ser Pro Cys Pro Gly Thr Ser Ser Thr Leu
      20      25      30
Thr Arg Thr Phe Phe Pro Ser Leu Val Ser Cys Val Gln Val Pro
      35      40      45
Phe Ser Trp Ile Pro Cys Leu Glu Cys Phe Leu Ile Tyr Phe Leu
      50      55      60
Ile Leu Ala Glu Asp Val Leu Gln Leu Phe Ser Gly Asn Ala Asn
      65      70      75
Met Gln Val Asn Gln

```



80

<210> 21  
 <211> 84  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1749147

<400> 21  
 Met Gln Arg Pro Phe Leu Ser Val Pro Cys Leu Leu Leu Leu Pro  
 1 5 10 15  
 Ala Arg Val Val Trp Gly Cys Trp Cys Phe Leu Pro Gly Glu Asp  
 20 25 30  
 Gly Gly Gly Cys Pro Thr Pro Ser Ser Gly Arg Ile Lys Leu Leu  
 35 40 45  
 Gln Gln Cys Leu Leu His Pro Ser Leu Arg Ser Ile Thr Val Ser  
 50 55 60  
 Arg Arg Ser Ala Gln Leu Leu Cys Arg Leu Lys Leu Gln Asn His  
 65 70 75  
 Ile Pro Lys Val Pro Gly Lys Asn Val  
 80

<210> 22  
 <211> 171  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1817722

<400> 22  
 Met His Met Ile Leu Lys Val Leu Thr Thr Ala Leu Leu Leu Gln  
 1 5 10 15  
 Ala Ala Ser Ala Leu Ala Asn Tyr Ile His Phe Ser Ser Tyr Ser  
 20 25 30  
 Lys Asp Gly Ile Gly Val Pro Phe Met Gly Ser Leu Ala Glu Phe  
 35 40 45  
 Phe Asp Ile Ala Ser Gln Ile Gln Met Leu Tyr Leu Leu Leu Ser  
 50 55 60  
 Leu Cys Met Gly Trp Thr Ile Val Arg Met Lys Lys Ser Gln Ser  
 65 70 75  
 Arg Pro Leu Gln Trp Asp Ser Thr Pro Ala Ser Thr Gly Ile Ala  
 80 85 90  
 Val Phe Ile Val Met Thr Gln Ser Val Leu Leu Leu Trp Glu Gln  
 95 100 105  
 Phe Glu Asp Ile Ser His His Ser Tyr His Ser His His Asn Leu  
 110 115 120

Ala Gly Ile Leu Leu Ile Val Leu Arg Ile Cys Leu Ala Leu Ser  
 125 130 135  
 Leu Gly Cys Gly Leu Tyr Gln Ile Ile Thr Val Glu Arg Ser Thr  
 140 145 150  
 Leu Lys Arg Glu Phe Tyr Ile Thr Phe Ala Lys Val Trp Val Trp  
 155 160 165  
 Lys Glu Asn Gly Leu Phe  
 170

&lt;210&gt; 23

&lt;211&gt; 243

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1831290

&lt;400&gt; 23

Met Ser Ser Gly Thr Glu Leu Leu Trp Pro Gly Ala Ala Leu Leu  
 1 5 10 15  
 Val Leu Leu Gly Val Ala Ala Ser Leu Cys Val Arg Cys Ser Arg  
 20 25 30  
 Pro Gly Ala Lys Arg Ser Glu Lys Ile Tyr Gln Gln Arg Ser Leu  
 35 40 45  
 Arg Glu Asp Gln Gln Ser Phe Thr Gly Ser Arg Thr Tyr Ser Leu  
 50 55 60  
 Val Gly Gln Ala Trp Pro Gly Pro Leu Ala Asp Met Ala Pro Thr  
 65 70 75  
 Arg Lys Asp Lys Leu Leu Gln Phe Tyr Pro Ser Leu Glu Asp Pro  
 80 85 90  
 Ala Ser Ser Arg Tyr Gln Asn Phe Ser Lys Gly Ser Arg His Gly  
 95 100 105  
 Ser Glu Glu Ala Tyr Ile Asp Pro Ile Ala Met Glu Tyr Tyr Asn  
 110 115 120  
 Trp Gly Arg Phe Ser Lys Pro Pro Glu Asp Asp Asp Ala Asn Ser  
 125 130 135  
 Tyr Glu Asn Val Leu Ile Cys Lys Gln Lys Thr Thr Glu Thr Gly  
 140 145 150  
 Ala Gln Gln Glu Gly Ile Gly Gly Leu Cys Arg Gly Asp Leu Ser  
 155 160 165  
 Leu Ser Leu Ala Leu Lys Thr Gly Pro Thr Ser Gly Leu Cys Pro  
 170 175 180  
 Ser Ala Ser Pro Glu Glu Asp Glu Glu Ser Glu Asp Tyr Gln Asn  
 185 190 195  
 Ser Ala Ser Ile His Gln Trp Arg Glu Ser Arg Lys Val Met Gly  
 200 205 210  
 Gln Leu Gln Arg Glu Ala Ser Pro Gly Pro Val Gly Ser Pro Asp  
 215 220 225  
 Glu Glu Asp Gly Glu Pro Asp Tyr Val Asn Gly Glu Val Ala Ala  
 230 235 240  
 Thr Glu Ala

```

<210> 24
<211> 311
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte Clone No: 1831477

<400> 24
Met Gly Val Pro Thr Ala Pro Glu Ala Gly Ser Trp Arg Trp Gly
 1           5           10           15
Ser Leu Leu Phe Ala Leu Phe Leu Ala Ala Ser Leu Gly Pro Val
 20           25           30
Ala Ala Phe Lys Val Ala Thr Pro Tyr Ser Leu Tyr Val Cys Pro
 35           40           45
Glu Gly Gln Asn Val Thr Leu Thr Cys Arg Leu Leu Gly Pro Val
 50           55           60
Asp Lys Gly His Asp Val Thr Phe Tyr Lys Thr Trp Tyr Arg Ser
 65           70           75
Ser Arg Gly Glu Val Gln Thr Cys Ser Glu Arg Arg Pro Ile Arg
 80           85           90
Asn Leu Thr Phe Gln Asp Leu His Leu His His Gly Gly His Gln
 95          100          105
Ala Ala Asn Thr Ser His Asp Leu Ala Gln Arg His Gly Leu Glu
110          115          120
Ser Ala Ser Asp His His Gly Asn Phe Ser Ile Thr Met Arg Asn
125          130          135
Leu Thr Leu Leu Asp Ser Gly Leu Tyr Cys Cys Leu Val Val Glu
140          145          150
Ile Arg His His His Ser Glu His Arg Val His Gly Ala Met Glu
155          160          165
Leu Gln Val Gln Thr Gly Lys Asp Ala Pro Ser Asn Cys Val Val
170          175          180
Tyr Pro Ser Ser Ser Gln Glu Ser Glu Asn Ile Thr Ala Ala Ala
185          190          195
Leu Ala Thr Gly Ala Cys Ile Val Gly Ile Leu Cys Leu Pro Leu
200          205          210
Ile Leu Leu Leu Val Tyr Lys Gln Arg Gln Ala Ala Ser Asn Arg
215          220          225
Arg Ala Gln Glu Leu Val Arg Met Asp Ser Asn Ile Gln Gly Ile
230          235          240
Glu Asn Pro Gly Phe Glu Ala Ser Pro Pro Ala Gln Gly Ile Pro
245          250          255
Glu Ala Lys Val Arg His Pro Leu Ser Tyr Val Ala Gln Arg Gln
260          265          270
Pro Ser Glu Ser Gly Arg His Leu Leu Ser Glu Pro Ser Thr Pro
275          280          285
Leu Ser Pro Pro Gly Pro Gly Asp Val Phe Phe Pro Ser Leu Asp
290          295          300
Pro Val Pro Asp Ser Pro Asn Phe Glu Val Ile
305          310

```

<210> 25  
<211> 57  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1841607

<400> 25  
Met Ala Ser Ser Cys Phe Ser Leu Ser Phe Pro Pro Leu Ser Leu  
1 5 10 15  
Ala Gly Ser Leu Ala Leu Trp Gly His Cys Cys Val Arg Leu Gly  
20 25 30  
Cys Ser Phe Trp Ser Val Ser Ala Met Ala Gln Arg Leu Pro Ser  
35 40 45  
Gln Asn Thr Tyr Asn Pro Pro Leu Cys Trp Ala Trp  
50 55

<210> 26  
<211> 82  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1852391

<400> 26  
Met Phe Ser Leu Phe Ser Cys Leu Leu Ala Cys Leu Leu Asp Leu  
1 5 10 15  
Leu Leu Ser Arg Val Ala Asp Glu Ala Phe Tyr Lys Gln Pro Phe  
20 25 30  
Ala Asp Val Ile Gly Tyr Val Tyr Val Ala Lys Leu Ile Pro Phe  
35 40 45  
Ser Thr Ser Asp Ser Phe Tyr Phe Cys Leu Glu Leu Met Leu Leu  
50 55 60  
Leu Cys His Gln Leu Leu Cys Phe Leu Asn Tyr Phe Lys Leu Ala  
65 70 75  
Leu Trp Gly Leu Pro Lys Asn  
80

<210> 27  
<211> 115  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1854555

&lt;400&gt; 27

```

Met Ala Gly Thr Val Leu Gly Val Gly Ala Gly Val Phe Ile Leu
 1           5           10           15
Ala Leu Leu Trp Val Ala Val Leu Leu Leu Cys Val Leu Leu Ser
           20           25           30
Arg Ala Ser Gly Ala Ala Arg Phe Ser Val Ile Phe Leu Phe Phe
           35           40           45
Gly Ala Val Ile Ile Thr Ser Val Leu Leu Leu Phe Pro Arg Ala
           50           55           60
Gly Glu Phe Pro Ala Pro Glu Val Glu Val Lys Ile Val Asp Asp
           65           70           75
Phe Phe Ile Gly Arg Tyr Val Leu Leu Ala Phe Leu Ser Ala Ile
           80           85           90
Phe Leu Gly Gly Leu Phe Leu Val Leu Ile His Tyr Val Leu Glu
           95          100          105
Pro Ile Tyr Ala Lys Pro Leu His Ser Tyr
           110          115

```

&lt;210&gt; 28

&lt;211&gt; 327

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1855755

&lt;400&gt; 28

```

Met Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly
 1           5           10           15
Phe Leu Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr
           20           25           30
Glu Pro Leu Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys
           35           40           45
Thr Tyr Ser Thr Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser
           50           55           60
Phe Val Gln Pro Gly Lys Pro Ile Ser Glu Ser His Pro Ile Leu
           65           70           75
Tyr Phe Thr Asn Gly His Leu Tyr Pro Thr Gly Ser Lys Ser Lys
           80           85           90
Arg Val Ser Leu Leu Gln Asn Pro Pro Thr Val Gly Val Ala Thr
           95          100          105
Leu Lys Leu Thr Asp Val His Pro Ser Asp Thr Gly Thr Tyr Leu
          110          115          120
Cys Gln Val Asn Asn Pro Pro Asp Phe Tyr Thr Asn Gly Leu Gly
          125          130          135
Leu Ile Asn Leu Thr Val Leu Val Pro Pro Ser Asn Pro Leu Cys
          140          145          150
Ser Gln Ser Gly Gln Thr Ser Val Gly Gly Ser Thr Ala Leu Arg
          155          160          165
Cys Ser Ser Ser Glu Gly Ala Pro Lys Pro Val Tyr Asn Trp Val
          170          175          180
Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser Met Val Gln
          185          190          195

```

```

Asp Glu Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser Leu Thr
      200                      205                      210
Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly Ser
      215                      220                      225
Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly
      230                      235                      240
Arg Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu
      245                      250                      255
Leu Ser Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg
      260                      265                      270
Gly Lys Lys Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu
      275                      280                      285
Asp Ala Ile Ala Pro Gly Ile Ser Glu His Thr Cys Met Arg Ala
      290                      295                      300
Asp Ser Ser Lys Gly Phe Leu Glu Arg Pro Ser Ser Ala Ser Thr
      305                      310                      315
Val Thr Thr Thr Lys Ser Lys Leu Pro Met Val Val
      320                      325

```

```

<210> 29
<211> 133
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 1861434

```

```

<400> 29
Met Arg Met Ser Leu Ala Gln Arg Val Leu Leu Thr Trp Leu Phe
  1          5          10          15
Thr Leu Leu Phe Leu Ile Met Leu Val Leu Lys Leu Asp Glu Lys
      20          25          30
Ala Pro Trp Asn Trp Phe Leu Ile Phe Ile Pro Val Trp Ile Phe
      35          40          45
Asp Thr Ile Leu Leu Val Leu Leu Ile Val Lys Met Ala Gly Arg
      50          55          60
Cys Lys Ser Gly Phe Asp Pro Arg His Gly Ser His Asn Ile Lys
      65          70          75
Lys Lys Ala Trp Tyr Leu Ile Ala Met Leu Leu Lys Leu Ala Phe
      80          85          90
Cys Leu Ala Leu Cys Ala Lys Leu Glu Gln Phe Thr Thr Met Asn
      95          100         105
Leu Ser Tyr Val Phe Ile Pro Leu Trp Ala Leu Leu Ala Gly Ala
      110         115         120
Leu Thr Glu Leu Gly Tyr Asn Val Phe Phe Val Arg Asp
      125         130

```

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<210> 30
<211> 129
<212> PRT

```

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1872334

&lt;400&gt; 30

```

Met Gly Leu Thr Leu Leu Leu Leu Leu Leu Gly Leu Glu Gly
 1           5           10           15
Gln Gly Ile Val Gly Ser Leu Pro Glu Val Leu Gln Ala Pro Val
          20           25           30
Gly Ser Ser Ile Leu Val Gln Cys His Tyr Arg Leu Gln Asp Val
          35           40           45
Lys Ala Gln Lys Val Trp Cys Arg Phe Leu Pro Glu Gly Cys Gln
          50           55           60
Pro Leu Val Ser Ser Ala Val Asp Arg Arg Ala Pro Ala Gly Arg
          65           70           75
Arg Thr Phe Leu Thr Asp Leu Gly Gly Gly Leu Leu Gln Val Glu
          80           85           90
Met Val Thr Leu Gln Glu Glu Asp Ala Gly Glu Tyr Gly Cys Met
          95          100          105
Val Asp Gly Ala Arg Gly Pro Gln Ile Leu His Arg Val Ser Leu
          110         115          120
Asn Ile Leu Pro Pro Gly Glu Leu Ser
          125

```

&lt;210&gt; 31

&lt;211&gt; 472

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1877230

&lt;400&gt; 31

```

Met Lys Phe Leu Ile Phe Ala Phe Phe Gly Gly Val His Leu Leu
 1           5           10           15
Ser Leu Cys Ser Gly Lys Ala Ile Cys Lys Asn Gly Ile Ser Lys
          20           25           30
Arg Thr Phe Glu Glu Ile Lys Glu Glu Ile Ala Ser Cys Gly Asp
          35           40           45
Val Ala Lys Ala Ile Ile Asn Leu Ala Val Tyr Gly Lys Ala Gln
          50           55           60
Asn Arg Ser Tyr Glu Arg Leu Ala Leu Leu Val Asp Thr Val Gly
          65           70           75
Pro Arg Leu Ser Gly Ser Lys Asn Leu Glu Lys Ala Ile Gln Ile
          80           85           90
Met Tyr Gln Asn Leu Gln Gln Asp Gly Leu Glu Lys Val His Leu
          95          100          105
Glu Pro Val Arg Ile Pro His Trp Glu Arg Gly Glu Glu Ser Ala
          110         115          120
Val Met Leu Glu Pro Arg Ile His Lys Ile Ala Ile Leu Gly Leu
          125         130          135

```

|                 |                     |                         |     |
|-----------------|---------------------|-------------------------|-----|
| Gly Ser Ser Ile | Gly Thr Pro Pro Glu | Gly Ile Thr Ala Glu Val |     |
|                 | 140                 | 145                     | 150 |
| Leu Val Val Thr | Ser Phe Asp Glu Leu | Gln Arg Arg Ala Ser Glu |     |
|                 | 155                 | 160                     | 165 |
| Ala Arg Gly Lys | Ile Val Val Tyr Asn | Gln Pro Tyr Ile Asn Tyr |     |
|                 | 170                 | 175                     | 180 |
| Ser Arg Thr Val | Gln Tyr Arg Thr Gln | Gly Ala Val Glu Ala Ala |     |
|                 | 185                 | 190                     | 195 |
| Lys Val Gly Ala | Leu Ala Ser Leu Ile | Arg Ser Val Ala Ser Phe |     |
|                 | 200                 | 205                     | 210 |
| Ser Ile Tyr Ser | Pro His Thr Gly Ile | Gln Glu Tyr Gln Asp Gly |     |
|                 | 215                 | 220                     | 225 |
| Val Pro Lys Ile | Pro Thr Ala Cys Ile | Thr Val Glu Asp Ala Glu |     |
|                 | 230                 | 235                     | 240 |
| Met Met Ser Arg | Met Ala Ser His Gly | Ile Lys Ile Val Ile Gln |     |
|                 | 245                 | 250                     | 255 |
| Leu Lys Met Gly | Ala Lys Thr Tyr Pro | Asp Thr Asp Ser Phe Asn |     |
|                 | 260                 | 265                     | 270 |
| Thr Val Ala Glu | Ile Thr Gly Ser Lys | Tyr Pro Glu Gln Val Val |     |
|                 | 275                 | 280                     | 285 |
| Leu Val Ser Gly | His Leu Asp Ser Trp | Asp Val Gly Gln Gly Ala |     |
|                 | 290                 | 295                     | 300 |
| Met Asp Asp Gly | Gly Gly Ala Phe Ile | Ser Trp Glu Ala Leu Ser |     |
|                 | 305                 | 310                     | 315 |
| Leu Ile Lys Asp | Leu Gly Leu Arg Pro | Lys Arg Thr Leu Arg Leu |     |
|                 | 320                 | 325                     | 330 |
| Val Leu Trp Thr | Ala Glu Glu Gln Gly | Gly Val Gly Ala Phe Gln |     |
|                 | 335                 | 340                     | 345 |
| Tyr Tyr Gln Leu | His Lys Val Asn Ile | Ser Asn Tyr Ser Leu Val |     |
|                 | 350                 | 355                     | 360 |
| Met Glu Ser Asp | Ala Gly Thr Phe Leu | Pro Thr Gly Leu Gln Phe |     |
|                 | 365                 | 370                     | 375 |
| Thr Gly Ser Glu | Lys Ala Arg Ala Ile | Met Glu Glu Val Met Ser |     |
|                 | 380                 | 385                     | 390 |
| Leu Leu Gln Pro | Leu Asn Ile Thr Gln | Val Leu Ser His Gly Glu |     |
|                 | 395                 | 400                     | 405 |
| Gly Thr Asp Ile | Asn Phe Trp Ile Gln | Ala Gly Val Pro Gly Ala |     |
|                 | 410                 | 415                     | 420 |
| Ser Leu Leu Asp | Asp Leu Tyr Lys Tyr | Phe Phe Phe His His Ser |     |
|                 | 425                 | 430                     | 435 |
| His Gly Asp Thr | Met Thr Val Met Asp | Pro Lys Gln Met Asn Val |     |
|                 | 440                 | 445                     | 450 |
| Ala Ala Ala Val | Trp Ala Val Val Ser | Tyr Val Val Ala Asp Met |     |
|                 | 455                 | 460                     | 465 |
| Glu Glu Met Leu | Pro Arg Ser         |                         |     |
|                 | 470                 |                         |     |

&lt;210&gt; 32

&lt;211&gt; 93

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature



&lt;223&gt; Incyte Clone No: 1877885

&lt;400&gt; 32

```

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val
  1           5           10           15
Ala Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala
          20           25           30
Phe Tyr Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu
          35           40           45
Ser Leu Pro Leu Leu Ala Gly Leu Val Ala Ala Asp Ala Val Ala
          50           55           60
Ser Leu Leu Ile Val Gly Ala Val Phe Leu Cys Ala Arg Pro Arg
          65           70           75
Arg Ser Pro Ala Gln Glu Asp Gly Lys Val Tyr Ile Asn Met Pro
          80           85           90
Gly Arg Gly

```

&lt;210&gt; 33

&lt;211&gt; 92

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1889269

&lt;400&gt; 33

```

Met Asn Arg Pro Ser Ala Arg Asn Ala Leu Gly Asn Val Phe Val
  1           5           10           15
Ser Glu Leu Leu Glu Thr Leu Ala Gln Leu Arg Glu Asp Arg Gln
          20           25           30
Val Arg Val Leu Leu Phe Arg Ser Gly Val Lys Gly Val Phe Cys
          35           40           45
Ala Gly Ala Asp Leu Lys Glu Arg Glu Gln Met Ser Glu Ala Glu
          50           55           60
Val Gly Val Phe Val Gln Arg Leu Arg Gly Leu Met Asn Asp Ile
          65           70           75
Gly Glu Asp Leu Gly Val Gly Trp Arg Arg Gly Phe Gly Gly Pro
          80           85           90
Cys Arg

```

&lt;210&gt; 34

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1890243

&lt;400&gt; 34

```

Met Trp Ile Lys Gly Thr Met Lys Met Arg Gly Gly Lys Thr Ser
 1           5           10           15
Arg Ser Ala Val Leu Pro Val Ala Gln Leu Thr Leu Ile Ala Ser
          20           25           30
Cys Phe Pro Asn Ser Gln Thr Val Leu Gly Thr Glu Gly Thr Leu
          35           40           45
Asp Val Glu Ser Ser Pro Leu Ala Leu Thr Gly Leu Trp Ala
          50           55           60
Ser Pro Glu Ser Leu Ser Leu Tyr Leu Val Thr Leu Leu Cys Val
          65           70           75
Cys Pro Ala Leu Gln Ser Cys Gln Gly Gln Gln Ala Asp Val Thr
          80           85           90
Leu Ala Pro Cys Glu Ile Phe Ile Pro Gln Thr Leu Ala Cys Glu
          95          100          105
Pro Phe Pro Ser Gln Trp Arg Ala Leu Lys Gly Ala Ser Leu Glu
          110          115          120
Ser Ser Ser Val Leu Trp Val Ala Pro Cys Arg Trp Pro Leu Thr
          125          130          135
Leu Arg Cys Ser Arg Val His Leu
          140

```

&lt;210&gt; 35

&lt;211&gt; 89

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1900433

&lt;400&gt; 35

```

Met Glu Arg Val Thr Leu Ala Leu Leu Leu Leu Ala Gly Leu Thr
 1           5           10           15
Ala Leu Glu Ala Asn Asp Pro Phe Ala Asn Lys Asp Asp Pro Phe
          20           25           30
Tyr Tyr Asp Trp Lys Asn Leu Gln Leu Ser Gly Leu Ile Cys Gly
          35           40           45
Gly Leu Leu Ala Ile Ala Gly Ile Ala Ala Val Leu Ser Gly Lys
          50           55           60
Cys Lys Tyr Lys Ser Ser Gln Lys Gln His Ser Pro Val Pro Glu
          65           70           75
Lys Ala Ile Pro Leu Ile Thr Pro Gly Ser Ala Thr Thr Cys
          80           85

```

&lt;210&gt; 36

&lt;211&gt; 560

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1909441

&lt;400&gt; 36

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Lys | Lys | Lys | Leu | Thr | Glu | Met | Ile | Pro | Leu | Cys | Asn | His |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |
| Pro | Ala | Ser | Phe | Val | Lys | Leu | Phe | Val | Ala | Leu | Gly | Pro | Ile | Ala |
|     |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |
| Gly | Pro | Glu | Glu | Lys | Lys | Gln | Leu | Lys | Ser | Thr | Met | Leu | Leu | Met |
|     |     |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |
| Ser | Glu | Asp | Leu | Thr | Gly | Glu | Gln | Ala | Leu | Ala | Val | Leu | Gly | Ala |
|     |     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |
| Met | Gly | Asp | Met | Glu | Ser | Arg | Asn | Ser | Cys | Leu | Ile | Lys | Arg | Val |
|     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |
| Thr | Ser | Val | Leu | His | Lys | His | Leu | Asp | Gly | Tyr | Lys | Pro | Leu | Glu |
|     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |
| Leu | Leu | Lys | Ile | Thr | Gln | Glu | Leu | Thr | Phe | Leu | His | Phe | Gln | Arg |
|     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |
| Lys | Glu | Phe | Phe | Ala | Lys | Leu | Arg | Glu | Leu | Leu | Leu | Ser | Tyr | Leu |
|     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |
| Lys | Asn | Ser | Phe | Ile | Pro | Thr | Glu | Val | Ser | Val | Leu | Val | Arg | Ala |
|     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |
| Ile | Ser | Leu | Leu | Pro | Ser | Pro | His | Leu | Asp | Glu | Val | Gly | Ile | Ser |
|     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |
| Arg | Ile | Glu | Ala | Val | Leu | Pro | Gln | Cys | Asp | Leu | Asn | Asn | Leu | Ser |
|     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |
| Ser | Phe | Ala | Thr | Ser | Val | Leu | Arg | Trp | Ile | Gln | His | Asp | His | Met |
|     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |
| Tyr | Leu | Asp | Asn | Met | Thr | Ala | Lys | Gln | Leu | Lys | Leu | Leu | Gln | Lys |
|     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |
| Leu | Asp | His | Tyr | Gly | Arg | Gln | Arg | Leu | Gln | His | Ser | Asn | Ser | Leu |
|     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |
| Asp | Leu | Leu | Arg | Lys | Glu | Leu | Lys | Ser | Leu | Lys | Gly | Asn | Thr | Phe |
|     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |
| Pro | Glu | Ser | Leu | Leu | Glu | Glu | Met | Ile | Ala | Thr | Leu | Gln | His | Phe |
|     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Met | Asp | Asp | Ile | Asn | Tyr | Ile | Asn | Val | Gly | Glu | Ile | Ala | Ser | Phe |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |
| Ile | Ser | Ser | Thr | Asp | Tyr | Leu | Ser | Thr | Leu | Leu | Leu | Asp | Arg | Ile |
|     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |
| Ala | Ser | Val | Ala | Val | Gln | Gln | Ile | Glu | Lys | Ile | His | Pro | Phe | Thr |
|     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |
| Ile | Pro | Ala | Ile | Ile | Arg | Pro | Phe | Ser | Val | Leu | Asn | Tyr | Asp | Pro |
|     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |
| Pro | Gln | Arg | Asp | Glu | Phe | Leu | Gly | Thr | Cys | Val | Gln | His | Leu | Asn |
|     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |
| Ser | Tyr | Leu | Gly | Ile | Leu | Asp | Pro | Phe | Ile | Leu | Val | Phe | Leu | Gly |
|     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |
| Phe | Ser | Leu | Ala | Thr | Leu | Glu | Tyr | Phe | Pro | Glu | Asp | Leu | Leu | Lys |
|     |     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |
| Ala | Ile | Phe | Asn | Ile | Lys | Phe | Leu | Ala | Arg | Leu | Asp | Ser | Gln | Leu |
|     |     |     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |
| Glu | Ile | Leu | Ser | Pro | Ser | Arg | Ser | Ala | Arg | Val | Gln | Phe | His | Leu |
|     |     |     |     | 365 |     |     |     |     | 370 |     |     |     |     | 375 |
| Met | Glu | Leu | Asn | Arg | Ser | Val | Cys | Leu | Glu | Cys | Pro | Glu | Phe | Gln |
|     |     |     |     | 380 |     |     |     |     | 385 |     |     |     |     | 390 |
| Ile | Pro | Trp | Phe | His | Asp | Arg | Phe | Cys | Gln | Gln | Tyr | Asn | Lys | Gly |
|     |     |     |     | 395 |     |     |     |     | 400 |     |     |     |     | 405 |

```

Ile Gly Gly Met Asp Gly Thr Gln Gln Gln Ile Phe Lys Met Leu
      410      415      420
Ala Glu Val Leu Gly Gly Ile Asn Cys Val Lys Ala Ser Val Leu
      425      430      435
Thr Pro Tyr Tyr His Lys Val Asp Phe Glu Cys Ile Leu Asp Lys
      440      445      450
Arg Lys Lys Pro Leu Pro Tyr Gly Ser His Asn Ile Ala Leu Gly
      455      460      465
Gln Leu Pro Glu Met Pro Trp Glu Ser Asn Ile Glu Ile Val Gly
      470      475      480
Ser Arg Leu Pro Pro Gly Ala Glu Arg Ile Ala Leu Glu Phe Leu
      485      490      495
Asp Ser Lys Ala Leu Cys Arg Asn Ile Pro His Met Lys Gly Lys
      500      505      510
Ser Ala Met Lys Lys Arg His Leu Glu Ile Leu Gly Tyr Arg Val
      515      520      525
Ile Gln Ile Ser Gln Phe Glu Trp Asn Ser Met Ala Leu Ser Thr
      530      535      540
Lys Asp Ala Arg Met Asp Tyr Leu Arg Glu Cys Ile Phe Gly Glu
      545      550      555
Val Lys Ser Cys Leu
      560

```

&lt;210&gt; 37

&lt;211&gt; 197

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1932226

&lt;400&gt; 37

```

Met Gly Val Pro Leu Gly Leu Gly Ala Ala Trp Leu Leu Ala Trp
  1      5      10      15
Pro Gly Leu Ala Leu Pro Leu Val Ala Met Ala Ala Gly Gly Arg
      20      25      30
Trp Val Arg Gln Gln Gly Pro Arg Val Arg Arg Gly Ile Ser Arg
      35      40      45
Leu Trp Leu Arg Val Leu Leu Arg Leu Ser Pro Met Ala Phe Arg
      50      55      60
Ala Leu Gln Gly Cys Gly Ala Val Gly Asp Arg Gly Leu Phe Ala
      65      70      75
Leu Tyr Pro Lys Thr Asn Lys Asp Gly Phe Arg Ser Arg Leu Pro
      80      85      90
Val Pro Gly Pro Arg Arg Arg Asn Pro Arg Thr Thr Gln His Pro
      95      100     105
Leu Ala Leu Leu Ala Arg Val Trp Val Leu Cys Lys Gly Trp Asn
      110     115     120
Trp Arg Leu Ala Arg Ala Ser Gln Gly Leu Ala Ser His Leu Pro
      125     130     135
Pro Trp Ala Ile His Thr Leu Ala Ser Trp Gly Leu Leu Arg Gly
      140     145     150
Glu Arg Pro Thr Arg Ile Pro Arg Leu Leu Pro Arg Ser Gln Arg

```

|                 |                     |                     |     |  |     |
|-----------------|---------------------|---------------------|-----|--|-----|
|                 | 155                 |                     | 160 |  | 165 |
| Gln Leu Gly Pro | Pro Ala Ser Arg Gln | Pro Leu Pro Gly Thr | Leu |  |     |
|                 | 170                 |                     | 175 |  | 180 |
| Ala Gly Arg Arg | Ser Arg Thr Arg Gln | Ser Arg Ala Leu Pro | Pro |  |     |
|                 | 185                 |                     | 190 |  | 195 |
| Trp Arg         |                     |                     |     |  |     |

&lt;210&gt; 38

&lt;211&gt; 437

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1932647

&lt;400&gt; 38

|                 |                     |                 |             |
|-----------------|---------------------|-----------------|-------------|
| Met Ser Ala Val | Leu Leu Leu Ala     | Leu Leu Gly Phe | Ile Leu Pro |
| 1               | 5                   | 10              | 15          |
| Leu Pro Gly Val | Gln Ala Leu Leu Cys | Gln Phe Gly Thr | Val Gln     |
|                 | 20                  | 25              | 30          |
| His Val Trp Lys | Val Ser Asp Leu Pro | Arg Gln Trp Thr | Pro Lys     |
|                 | 35                  | 40              | 45          |
| Asn Thr Ser Cys | Asp Ser Gly Leu Gly | Cys Gln Asp Thr | Leu Met     |
|                 | 50                  | 55              | 60          |
| Leu Ile Glu Ser | Gly Pro Gln Val Ser | Leu Val Leu Ser | Lys Gly     |
|                 | 65                  | 70              | 75          |
| Cys Thr Glu Ala | Lys Asp Gln Glu Pro | Arg Val Thr Glu | His Arg     |
|                 | 80                  | 85              | 90          |
| Met Gly Pro Gly | Leu Ser Leu Ile Ser | Tyr Thr Phe Val | Cys Arg     |
|                 | 95                  | 100             | 105         |
| Gln Glu Asp Phe | Cys Asn Asn Leu Val | Asn Ser Leu Pro | Leu Trp     |
|                 | 110                 | 115             | 120         |
| Ala Pro Gln Pro | Pro Ala Asp Pro Gly | Ser Leu Arg Cys | Pro Val     |
|                 | 125                 | 130             | 135         |
| Cys Leu Ser Met | Glu Gly Cys Leu Glu | Gly Thr Thr Glu | Glu Ile     |
|                 | 140                 | 145             | 150         |
| Cys Pro Lys Gly | Thr Thr His Cys Tyr | Asp Gly Leu Leu | Arg Leu     |
|                 | 155                 | 160             | 165         |
| Arg Gly Gly Gly | Ile Phe Ser Asn Leu | Arg Val Gln Gly | Cys Met     |
|                 | 170                 | 175             | 180         |
| Pro Gln Pro Gly | Cys Asn Leu Leu Asn | Gly Thr Gln Glu | Ile Gly     |
|                 | 185                 | 190             | 195         |
| Pro Val Gly Met | Thr Glu Asn Cys Asn | Arg Lys Asp Phe | Leu Thr     |
|                 | 200                 | 205             | 210         |
| Cys His Arg Gly | Thr Thr Ile Met Thr | His Gly Asn Leu | Ala Gln     |
|                 | 215                 | 220             | 225         |
| Glu Pro Thr Asp | Trp Thr Thr Ser Asn | Thr Glu Met Cys | Glu Val     |
|                 | 230                 | 235             | 240         |
| Gly Gln Val Cys | Gln Glu Thr Leu Leu | Leu Ile Asp Val | Gly Leu     |
|                 | 245                 | 250             | 255         |
| Thr Ser Thr Leu | Val Gly Thr Lys Gly | Cys Ser Thr Val | Gly Ala     |
|                 | 260                 | 265             | 270         |
| Gln Asn Ser Gln | Lys Thr Thr Ile His | Ser Ala Pro Pro | Gly Val     |

|                 |                     |                     |     |  |     |
|-----------------|---------------------|---------------------|-----|--|-----|
|                 | 275                 |                     | 280 |  | 285 |
| Leu Val Ala Ser | Tyr Thr His Phe Cys | Ser Ser Asp Leu Cys | Asn |  |     |
|                 | 290                 |                     | 295 |  | 300 |
| Ser Ala Ser Ser | Ser Ser Val Leu Leu | Asn Ser Leu Pro Pro | Gln |  |     |
|                 | 305                 |                     | 310 |  | 315 |
| Ala Ala Pro Val | Pro Gly Asp Arg Gln | Cys Pro Thr Cys Val | Gln |  |     |
|                 | 320                 |                     | 325 |  | 330 |
| Pro Leu Gly Thr | Cys Ser Ser Gly Ser | Pro Arg Met Thr Cys | Pro |  |     |
|                 | 335                 |                     | 340 |  | 345 |
| Arg Gly Ala Thr | His Cys Tyr Asp Gly | Tyr Ile His Leu Ser | Gly |  |     |
|                 | 350                 |                     | 355 |  | 360 |
| Gly Gly Leu Ser | Thr Lys Met Ser Ile | Gln Gly Cys Val Ala | Gln |  |     |
|                 | 365                 |                     | 370 |  | 375 |
| Pro Ser Ser Phe | Leu Leu Asn His Thr | Arg Gln Ile Gly Ile | Phe |  |     |
|                 | 380                 |                     | 385 |  | 390 |
| Ser Ala Arg Glu | Lys Arg Asp Val Gln | Pro Pro Ala Ser Gln | His |  |     |
|                 | 395                 |                     | 400 |  | 405 |
| Glu Gly Gly Gly | Ala Glu Gly Leu Glu | Ser Leu Thr Trp Gly | Val |  |     |
|                 | 410                 |                     | 415 |  | 420 |
| Gly Leu Ala Leu | Ala Pro Ala Leu Trp | Trp Gly Val Val Cys | Pro |  |     |
|                 | 425                 |                     | 430 |  | 435 |
| Ser Cys         |                     |                     |     |  |     |

&lt;210&gt; 39

&lt;211&gt; 330

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2124245

&lt;400&gt; 39

|                 |                 |                 |             |
|-----------------|-----------------|-----------------|-------------|
| Met Glu Gly Ala | Pro Pro Gly Ser | Leu Ala Leu Arg | Leu Leu Leu |
| 1               | 5               | 10              | 15          |
| Phe Val Ala Leu | Pro Ala Ser Gly | Trp Leu Thr Thr | Gly Ala Pro |
|                 | 20              | 25              | 30          |
| Glu Pro Pro Pro | Leu Ser Gly Ala | Pro Gln Asp Gly | Ile Arg Ile |
|                 | 35              | 40              | 45          |
| Asn Val Thr Thr | Leu Lys Asp Asp | Gly Asp Ile Ser | Lys Gln Gln |
|                 | 50              | 55              | 60          |
| Val Val Leu Asn | Ile Thr Tyr Glu | Ser Gly Gln Val | Tyr Val Asn |
|                 | 65              | 70              | 75          |
| Asp Leu Pro Val | Asn Ser Gly Val | Thr Arg Ile Ser | Cys Gln Thr |
|                 | 80              | 85              | 90          |
| Leu Ile Val Lys | Asn Glu Asn Leu | Glu Asn Leu Glu | Glu Lys Glu |
|                 | 95              | 100             | 105         |
| Tyr Phe Gly Ile | Val Ser Val Arg | Ile Leu Val His | Glu Trp Pro |
|                 | 110             | 115             | 120         |
| Met Thr Ser Gly | Ser Ser Leu Gln | Leu Ile Val Ile | Gln Glu Glu |
|                 | 125             | 130             | 135         |
| Val Val Glu Ile | Asp Gly Lys Gln | Val Gln Gln Lys | Asp Val Thr |
|                 | 140             | 145             | 150         |
| Glu Ile Asp Ile | Leu Val Lys Asn | Arg Gly Val Leu | Arg His Ser |

|                 |                     |                     |     |  |     |
|-----------------|---------------------|---------------------|-----|--|-----|
|                 | 155                 |                     | 160 |  | 165 |
| Asn Tyr Thr Leu | Pro Leu Glu Glu Ser | Met Leu Tyr Ser Ile | Ser |  |     |
|                 | 170                 |                     | 175 |  | 180 |
| Arg Asp Ser Asp | Ile Leu Phe Thr Leu | Pro Asn Leu Ser Lys | Lys |  |     |
|                 | 185                 |                     | 190 |  | 195 |
| Glu Ser Val Ser | Ser Leu Gln Thr Thr | Ser Gln Tyr Leu Ile | Arg |  |     |
|                 | 200                 |                     | 205 |  | 210 |
| Asn Val Glu Thr | Thr Val Asp Glu Asp | Val Leu Pro Gly Lys | Leu |  |     |
|                 | 215                 |                     | 220 |  | 225 |
| Pro Glu Thr Pro | Leu Arg Ala Glu Pro | Pro Ser Ser Tyr Lys | Val |  |     |
|                 | 230                 |                     | 235 |  | 240 |
| Met Cys Gln Trp | Met Glu Lys Phe Arg | Lys Asp Leu Cys Arg | Phe |  |     |
|                 | 245                 |                     | 250 |  | 255 |
| Trp Ser Asn Val | Phe Pro Val Phe Phe | Gln Phe Leu Asn Ile | Met |  |     |
|                 | 260                 |                     | 265 |  | 270 |
| Val Val Gly Ile | Thr Gly Ala Ala Val | Val Ile Thr Ile Leu | Lys |  |     |
|                 | 275                 |                     | 280 |  | 285 |
| Val Phe Phe Pro | Val Ser Glu Tyr Lys | Gly Ile Leu Gln Leu | Asp |  |     |
|                 | 290                 |                     | 295 |  | 300 |
| Lys Val Asp Val | Ile Pro Val Thr Ala | Ile Asn Leu Tyr Pro | Asp |  |     |
|                 | 305                 |                     | 310 |  | 315 |
| Gly Pro Glu Lys | Arg Ala Glu Asn Leu | Glu Asp Lys Thr Cys | Ile |  |     |
|                 | 320                 |                     | 325 |  | 330 |

&lt;210&gt; 40

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2132626

&lt;400&gt; 40

|   |     |     |
|---|-----|-----|
| Met Glu Thr Gly Ala Leu Arg Arg Pro Gln Leu Leu Pro Leu Leu |     |     |
| 1   | 5   | 10  |
| Leu Leu Leu Cys Gly Gly Cys Pro Arg Ala Gly Gly Cys Asn Glu |     | 15  |
|   | 20  | 25  |
| Thr Gly Met Leu Glu Arg Leu Pro Leu Cys Gly Lys Ala Phe Ala |     | 30  |
|   | 35  | 40  |
| Asp Met Met Gly Lys Val Asp Val Trp Lys Trp Cys Asn Leu Ser |     | 45  |
|   | 50  | 55  |
| Glu Phe Ile Val Tyr Tyr Glu Ser Phe Thr Asn Cys Thr Glu Met |     | 60  |
|   | 65  | 70  |
| Glu Ala Asn Val Val Gly Cys Tyr Trp Pro Asn Pro Leu Ala Gln |     | 75  |
|   | 80  | 85  |
| Gly Phe Ile Thr Gly Ile His Arg Gln Phe Phe Ser Asn Cys Thr |     | 90  |
|   | 95  | 100 |
| Val Asp Arg Val His Leu Glu Asp Pro Pro Asp Glu Val Leu Ile |     | 105 |
|   | 110 | 115 |
| Pro Leu Ile Val Ile Pro Val Val Leu Thr Val Ala Met Ala Gly |     | 120 |
|   | 125 | 130 |
| Leu Val Val Trp Arg Ser Lys Arg Thr Asp Thr Leu Leu         |     | 135 |
|   | 140 | 145 |

<210> 41  
 <211> 188  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2280639

<400> 41  
 Met Ala Pro Pro Pro Ser Pro Gln Leu Leu Leu Ala Ala  
 1 5 10 15  
 Leu Ala Arg Leu Leu Gly Pro Ser Glu Val Met Ala Gly Pro Ala  
 20 25 30  
 Glu Glu Ala Gly Ala His Cys Pro Glu Ser Leu Trp Pro Leu Pro  
 35 40 45  
 Pro Gln Val Ser Pro Arg Val Thr Tyr Thr Arg Val Ser Pro Gly  
 50 55 60  
 Gln Ala Glu Asp Val Thr Phe Leu Tyr His Pro Cys Ala His Pro  
 65 70 75  
 Trp Leu Lys Leu Gln Leu Ala Leu Leu Ala Tyr Ala Cys Met Ala  
 80 85 90  
 Asn Pro Ser Leu Thr Pro Asp Phe Ser Leu Thr Gln Asp Arg Pro  
 95 100 105  
 Leu Val Leu Thr Ala Trp Gly Leu Ala Leu Glu Met Ala Trp Val  
 110 115 120  
 Glu Pro Ala Trp Ala Ala His Trp Leu Met Arg Arg Arg Arg Arg  
 125 130 135  
 Lys Gln Arg Lys Lys Lys Ala Trp Ile Tyr Cys Glu Ser Leu Ser  
 140 145 150  
 Gly Pro Ala Pro Ser Glu Pro Thr Pro Gly Arg Gly Arg Leu Cys  
 155 160 165  
 Arg Arg Gly Cys Val Gln Ala Leu Ala Leu Ala Phe Ala Leu Arg  
 170 175 180  
 Thr Gly Gly Pro Leu Ala Gln Arg  
 185

<210> 42  
 <211> 222  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2292356

<400> 42  
 Met Ala Ala Ala Ala Leu Thr Ser Leu Ser Thr Ser Pro Leu Leu  
 1 5 10 15  
 Leu Gly Ala Pro Val Ala Ala Phe Ser Pro Glu Pro Gly Leu Glu  
 20 25 30



```

Pro Trp Lys Glu Ala Leu Val Arg Pro Pro Gly Ser Tyr Ser Ser
      35                      40                      45
Ser Ser Asn Ser Gly Asp Trp Gly Trp Asp Leu Ala Ser Asp Gln
      50                      55                      60
Ser Ser Pro Ser Thr Pro Ser Pro Pro Leu Pro Pro Glu Ala Ala
      65                      70                      75
His Phe Leu Phe Gly Glu Pro Thr Leu Arg Lys Arg Lys Ser Pro
      80                      85                      90
Ala Gln Val Met Phe Gln Cys Leu Trp Lys Ser Cys Gly Lys Val
      95                      100                     105
Leu Ser Thr Ala Ser Ala Met Gln Arg His Ile Arg Leu Val His
     110                      115                     120
Leu Gly Cys Gly Gly Ala Trp Gly Ala Ala Gly Pro Ala Gly Trp
     125                      130                     135
Leu Gly Leu Leu Gly Pro Ala Arg Pro Pro Leu Gln Leu Pro Leu
     140                      145                     150
Ala Gly Cys Val Ser Arg Arg Arg Gln Ala Glu Pro Glu Gln Ser
     155                      160                     165
Asp Gly Glu Glu Asp Phe Tyr Tyr Thr Glu Leu Asp Val Gly Val
     170                      175                     180
Asp Thr Leu Thr Asp Gly Leu Ser Ser Leu Thr Pro Val Phe Pro
     185                      190                     195
Glu Gly Phe His Ala Ser Leu Pro Ser Pro Ala Leu Lys Leu Arg
     200                      205                     210
Arg Leu Gly Gly Thr Arg Gln Pro Arg Gln Tyr Pro
     215                      220

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&lt;210&gt; 43

&lt;211&gt; 111

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2349310

&lt;400&gt; 43

```

Met Gly Pro Ser Ser Cys Leu Leu Leu Ile Leu Ile Pro Leu Leu
  1                      5                      10                     15
Gln Leu Ile Asn Leu Gly Ser Thr Gln Cys Ser Leu Asp Ser Val
      20                      25                      30
Met Asp Lys Lys Ile Lys Asp Val Leu Asn Ser Leu Glu Tyr Ser
      35                      40                      45
Pro Ser Pro Ile Ser Lys Lys Leu Ser Cys Ala Ser Val Lys Ser
      50                      55                      60
Gln Gly Arg Pro Ser Ser Cys Pro Ala Gly Met Ala Val Thr Gly
      65                      70                      75
Cys Ala Cys Gly Tyr Gly Cys Gly Ser Trp Asp Val Gln Leu Glu
      80                      85                      90
Thr Thr Cys His Cys Gln Cys Ser Val Val Asp Trp Thr Thr Ala
      95                      100                     105
Arg Cys Cys His Leu Thr
      110

```

<210> 44  
 <211> 341  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2373227

<400> 44  
 Met Val Pro Ala Ala Gly Ala Leu Leu Trp Val Leu Leu Leu Asn  
 1 5 10 15  
 Leu Gly Pro Arg Ala Ala Gly Ala Gln Gly Leu Thr Gln Thr Pro  
 20 25 30  
 Thr Glu Met Gln Arg Val Ser Leu Arg Phe Gly Gly Pro Met Thr  
 35 40 45  
 Arg Ser Tyr Arg Ser Thr Ala Arg Thr Gly Leu Pro Arg Lys Thr  
 50 55 60  
 Arg Ile Ile Leu Glu Asp Glu Asn Asp Ala Met Ala Asp Ala Asp  
 65 70 75  
 Arg Leu Ala Gly Pro Ala Ala Ala Glu Leu Leu Ala Ala Thr Val  
 80 85 90  
 Ser Thr Gly Phe Ser Arg Ser Ser Ala Ile Asn Glu Glu Asp Gly  
 95 100 105  
 Ser Ser Glu Glu Gly Val Val Ile Asn Ala Gly Lys Asp Ser Thr  
 110 115 120  
 Ser Arg Glu Leu Pro Ser Ala Thr Pro Asn Thr Ala Gly Ser Ser  
 125 130 135  
 Ser Thr Arg Phe Ile Ala Asn Ser Gln Glu Pro Glu Ile Arg Leu  
 140 145 150  
 Thr Ser Ser Leu Pro Arg Ser Pro Gly Arg Ser Thr Glu Asp Leu  
 155 160 165  
 Pro Gly Ser Gln Ala Thr Leu Ser Gln Trp Ser Thr Pro Gly Ser  
 170 175 180  
 Thr Pro Ser Arg Trp Pro Ser Pro Ser Pro Thr Ala Met Pro Ser  
 185 190 195  
 Pro Glu Asp Leu Arg Leu Val Leu Met Pro Trp Gly Pro Trp His  
 200 205 210  
 Cys His Cys Lys Ser Gly Thr Met Ser Arg Ser Arg Ser Gly Lys  
 215 220 225  
 Leu His Gly Leu Ser Gly Arg Leu Arg Val Gly Ala Leu Ser Gln  
 230 235 240  
 Leu Arg Thr Glu His Lys Pro Cys Thr Tyr Gln Gln Cys Pro Cys  
 245 250 255  
 Asn Arg Leu Arg Glu Glu Cys Pro Leu Asp Thr Ser Leu Cys Thr  
 260 265 270  
 Asp Thr Asn Cys Ala Ser Gln Ser Thr Thr Ser Thr Arg Thr Thr  
 275 280 285  
 Thr Thr Pro Phe Pro Thr Ile His Leu Arg Ser Ser Pro Ser Leu  
 290 295 300  
 Pro Pro Ala Ser Pro Cys Pro Ala Leu Ala Phe Trp Lys Arg Val  
 305 310 315  
 Arg Ile Gly Leu Glu Asp Ile Trp Asn Ser Leu Ser Ser Val Phe  
 320 325 330  
 Thr Glu Met Gln Pro Ile Asp Arg Asn Gln Arg

335

340

<210> 45  
 <211> 148  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2457682

<400> 45  
 Met Ala Gly Leu Ala Ala Arg Leu Val Leu Leu Ala Gly Ala Ala  
   1                  5                  10                  15  
 Ala Leu Ala Ser Gly Ser Gln Gly Asp Arg Glu Pro Val Tyr Arg  
                   20                  25                  30  
 Asp Cys Val Leu Gln Cys Glu Glu Gln Asn Cys Ser Gly Gly Ala  
                   35                  40                  45  
 Leu Asn His Phe Arg Ser Arg Gln Pro Ile Tyr Met Ser Leu Ala  
                   50                  55                  60  
 Gly Trp Thr Cys Arg Asp Asp Cys Lys Tyr Glu Cys Met Trp Val  
                   65                  70                  75  
 Thr Val Gly Leu Tyr Leu Gln Glu Gly His Lys Val Pro Gln Phe  
                   80                  85                  90  
 His Gly Lys Trp Pro Phe Ser Arg Phe Leu Phe Phe Gln Glu Pro  
                   95                  100                  105  
 Ala Ser Ala Val Ala Ser Phe Leu Asn Gly Leu Ala Ser Leu Val  
                   110                  115                  120  
 Met Leu Cys Arg Tyr Arg Thr Phe Val Pro Ala Ser Ser Pro Met  
                   125                  130                  135  
 Tyr His Thr Cys Val Ala Phe Ala Trp Leu Ser Gly Arg  
                   140                  145

<210> 46  
 <211> 87  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2480426

<400> 46  
 Met Arg Pro Leu Leu Val Leu Leu Leu Leu Gly Leu Ala Ala Gly  
   1                  5                  10                  15  
 Ser Pro Pro Leu Asp Asp Asn Lys Ile Pro Ser Leu Cys Pro Gly  
                   20                  25                  30  
 Leu Pro Gly Pro Arg Gly Asp Pro Gly Pro Arg Gly Glu Ala Gly  
                   35                  40                  45  
 Pro Ala Gly Pro Thr Gly Leu Ala Gly Glu Cys Ser Val Pro Pro  
                   50                  55                  60

Arg Ser Ala Phe Ser Ala Lys Arg Ser Glu Ile Arg Val Pro Pro  
                   65                  70                  75  
 Leu Ser Asp Ala Pro Leu Pro Ser Thr Ala Cys Trp  
                   80                  85

<210> 47  
 <211> 383  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2503743

<400> 47  
 Met Ala Gly Ile Pro Gly Leu Leu Phe Leu Leu Phe Phe Leu Leu  
   1                  5                  10                  15  
 Cys Ala Val Gly Gln Val Ser Pro Tyr Ser Ala Pro Trp Lys Pro  
                   20                  25                  30  
 Thr Trp Pro Ala Tyr Arg Leu Pro Val Val Leu Pro Gln Ser Thr  
                   35                  40                  45  
 Leu Asn Leu Ala Lys Pro Asp Phe Gly Ala Glu Ala Lys Leu Glu  
                   50                  55                  60  
 Val Ser Ser Ser Cys Gly Pro Gln Cys His Lys Gly Thr Pro Leu  
                   65                  70                  75  
 Pro Thr Tyr Glu Glu Ala Lys Gln Tyr Leu Ser Tyr Glu Thr Leu  
                   80                  85                  90  
 Tyr Ala Asn Gly Ser Arg Thr Glu Thr Gln Val Gly Ile Tyr Ile  
                   95                  100                 105  
 Leu Ser Ser Ser Gly Asp Gly Ala Gln His Arg Asp Ser Gly Ser  
                  110                 115                 120  
 Ser Gly Lys Ser Arg Arg Lys Arg Gln Ile Tyr Gly Tyr Asp Ser  
                  125                 130                 135  
 Arg Phe Ser Ile Phe Gly Lys Asp Phe Leu Leu Asn Tyr Pro Phe  
                  140                 145                 150  
 Ser Thr Ser Val Lys Leu Ser Thr Gly Cys Thr Gly Thr Leu Val  
                  155                 160                 165  
 Ala Glu Lys His Val Leu Thr Ala Ala His Cys Ile His Asp Gly  
                  170                 175                 180  
 Lys Thr Tyr Val Lys Gly Thr Gln Lys Leu Arg Val Gly Phe Leu  
                  185                 190                 195  
 Lys Pro Lys Phe Lys Asp Gly Gly Arg Gly Ala Asn Asp Ser Thr  
                  200                 205                 210  
 Ser Ala Met Pro Glu Gln Met Lys Phe Gln Trp Ile Arg Val Lys  
                  215                 220                 225  
 Arg Thr His Val Pro Lys Gly Trp Ile Lys Gly Asn Ala Asn Asp  
                  230                 235                 240  
 Ile Gly Met Asp Tyr Asp Tyr Ala Leu Leu Glu Leu Lys Lys Pro  
                  245                 250                 255  
 His Lys Arg Lys Phe Met Lys Ile Gly Val Ser Pro Pro Ala Lys  
                  260                 265                 270  
 Gln Leu Pro Gly Gly Arg Ile His Phe Ser Gly Tyr Asp Asn Asp  
                  275                 280                 285  
 Arg Pro Gly Asn Leu Val Tyr Arg Phe Cys Asp Val Lys Asp Glu

|                 |   |     |
|-----------------|---|-----|
| 290             | 295   | 300 |
| Thr Tyr Asp Leu | Leu Tyr Gln Gln Cys Asp Ala Gln Pro Gly Ala |     |
| 305             | 310   | 315 |
| Ser Gly Ser Gly | Val Tyr Val Arg Met Trp Lys Arg Gln Gln Gln |     |
| 320             | 325   | 330 |
| Lys Trp Glu Arg | Lys Ile Ile Gly Ile Phe Ser Gly His Gln Trp |     |
| 335             | 340   | 345 |
| Val Asp Met Asn | Gly Ser Pro Gln Asp Phe Asn Val Ala Val Arg |     |
| 350             | 355   | 360 |
| Ile Thr Pro Leu | Lys Tyr Ala Gln Ile Cys Tyr Trp Ile Lys Gly |     |
| 365             | 370   | 375 |
| Asn Tyr Leu Asp | Cys Arg Glu Gly                             |     |
| 380             |   |     |

&lt;210&gt; 48

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2537684

&lt;400&gt; 48

|                 |   |     |
|-----------------|---|-----|
| Met Leu Leu Pro | Ala Leu Cys Ala Trp Leu Leu Trp Val Pro Trp |     |
| 1               | 5   | 10  |
| Cys Leu Leu Val | Ala Gly Ser Gly Arg Ser Gly Gly Glu Leu Cys | 15  |
| 20              | 25  | 30  |
| Cys Ser Ser Tyr | Gly Val Ser Val Ile Ser Val Trp Ser Lys Cys |     |
| 35              | 40  | 45  |
| Ser Val Cys Arg | Cys Leu Met Gly Ser Val Pro Arg Ile Phe Phe |     |
| 50              | 55  | 60  |
| Ala Phe Tyr Pro | Ile Ala Trp Leu Pro Leu Pro Gly Ser Gln Gly |     |
| 65              | 70  | 75  |
| Cys Trp Ser Arg | Ser Trp Glu Trp Pro Leu Val Glu Pro Ala Ser |     |
| 80              | 85  | 90  |
| Cys Leu Val Cys | Leu Cys Phe Thr Phe Gly Val Leu Ser Gly Val |     |
| 95              | 100   | 105 |
| Val Ala Val Lys |   |     |

&lt;210&gt; 49

&lt;211&gt; 185

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2593853

&lt;400&gt; 49

Met Lys Phe Thr Ile Val Phe Ala Gly Leu Leu Gly Val Phe Leu

```

1           5           10           15
Ala Pro Ala Leu Ala Asn Tyr Asn Ile Asn Val Asn Asp Asp Asn
20           25           30
Asn Asn Ala Gly Ser Gly Gln Gln Ser Val Ser Val Asn Asn Glu
35           40           45
His Asn Val Ala Asn Val Asp Asn Asn Asn Gly Trp Asp Ser Trp
50           55           60
Asn Ser Ile Trp Asp Tyr Gly Asn Gly Phe Ala Ala Thr Arg Leu
65           70           75
Phe Gln Lys Lys Thr Cys Ile Val His Lys Met Asn Lys Glu Val
80           85           90
Met Pro Ser Ile Gln Ser Leu Asp Ala Leu Val Lys Glu Lys Lys
95           100          105
Leu Gln Gly Lys Gly Pro Gly Gly Pro Pro Pro Lys Gly Leu Met
110          115          120
Tyr Ser Val Asn Pro Asn Lys Val Asp Asp Leu Ser Lys Phe Gly
125          130          135
Lys Asn Ile Ala Asn Met Cys Arg Gly Ile Pro Thr Tyr Met Ala
140          145          150
Glu Glu Met Gln Glu Ala Ser Leu Phe Phe Tyr Ser Gly Thr Cys
155          160          165
Tyr Thr Thr Ser Val Leu Trp Ile Val Asp Ile Ser Phe Cys Gly
170          175          180
Asp Thr Val Glu Asn
185

```

&lt;210&gt; 50

&lt;211&gt; 110

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2622354

&lt;400&gt; 50

```

Met Ala Pro Arg Gly Cys Ile Val Ala Val Phe Ala Ile Phe Cys
1           5           10           15
Ile Ser Arg Leu Leu Cys Ser His Gly Ala Pro Val Ala Pro Met
20           25           30
Thr Pro Tyr Leu Met Leu Cys Gln Pro His Lys Arg Cys Gly Asp
35           40           45
Lys Phe Tyr Asp Pro Leu Gln His Cys Cys Tyr Asp Asp Ala Val
50           55           60
Val Pro Leu Ala Arg Thr Gln Thr Cys Gly Asn Cys Thr Phe Arg
65           70           75
Val Cys Phe Glu Gln Cys Cys Pro Trp Thr Phe Met Val Lys Leu
80           85           90
Ile Asn Gln Asn Cys Asp Ser Ala Arg Thr Ser Asp Asp Arg Leu
95           100          105
Cys Arg Ser Val Ser
110

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<210> 51  
 <211> 126  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2641377

<400> 51  
 Met Trp Leu Gly Ser Trp Leu Thr Ser Leu Leu Leu Ser Pro Tyr  
     1                    5                    10                    15  
 Gly Ser Gly Trp Glu Lys Val Pro Cys Cys Val Thr Gly His Leu  
                     20                    25                    30  
 Arg Ser Cys Ser Cys Cys Leu Leu Gly Leu Ala Gly Val Gln Ser  
                     35                    40                    45  
 Asp His Phe Ser Glu Gly Phe Phe Ser Glu Tyr Ser Ser Asp Val  
                     50                    55                    60  
 Leu Pro Trp Gly Arg Arg Ser Phe Leu Pro Gln Gly Asp Ala Ser  
                     65                    70                    75  
 Leu Leu Ala Cys Glu Cys Phe Leu His Leu Gln Val Val Trp Gly  
                     80                    85                    90  
 Gln Phe Cys Leu Leu Glu Ala Trp Ala Gly Phe Thr Glu Gly Ser  
                     95                    100                    105  
 Met Pro Ala Pro Ser Cys Arg Val His Phe Trp Cys Arg Val Asn  
                     110                    115                    120  
 Thr Cys Ala Phe Met Ser  
                     125

<210> 52  
 <211> 488  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2674857

<400> 52  
 Met Ala Gly Lys Gly Ser Ser Gly Arg Arg Pro Leu Leu Leu Gly  
     1                    5                    10                    15  
 Leu Leu Val Ala Val Ala Thr Val His Leu Val Ile Cys Pro Tyr  
                     20                    25                    30  
 Thr Lys Val Glu Glu Ser Phe Asn Leu Gln Ala Thr His Asp Leu  
                     35                    40                    45  
 Leu Tyr His Trp Gln Asp Leu Glu Gln Tyr Asp His Leu Glu Phe  
                     50                    55                    60  
 Pro Gly Val Val Pro Arg Thr Phe Leu Gly Pro Val Val Ile Ala  
                     65                    70                    75  
 Val Phe Ser Ser Pro Ala Val Tyr Val Leu Ser Leu Leu Glu Met  
                     80                    85                    90  
 Ser Lys Phe Tyr Ser Gln Leu Ile Val Arg Gly Val Leu Gly Leu  
                     95                    100                    105

|                 |   |     |     |     |
|-----------------|---|-----|-----|-----|
| Gly Val Ile Phe | Gly Leu Trp Thr Leu Gln Lys Glu Val Arg Arg | 110 | 115 | 120 |
| His Phe Gly Ala | Met Val Ala Thr Met Phe Cys Trp Val Thr Ala | 125 | 130 | 135 |
| Met Gln Phe His | Leu Met Phe Tyr Cys Thr Arg Thr Leu Pro Asn | 140 | 145 | 150 |
| Val Leu Ala Leu | Pro Val Val Leu Leu Ala Leu Ala Ala Trp Leu | 155 | 160 | 165 |
| Arg His Glu Trp | Ala Arg Phe Ile Trp Leu Ser Ala Phe Ala Ile | 170 | 175 | 180 |
| Ile Val Phe Arg | Val Glu Leu Cys Leu Phe Leu Gly Leu Leu Leu | 185 | 190 | 195 |
| Leu Leu Ala Leu | Gly Asn Arg Lys Val Ser Val Val Arg Ala Leu | 200 | 205 | 210 |
| Arg His Ala Val | Pro Ala Gly Ile Leu Cys Leu Gly Leu Thr Val | 215 | 220 | 225 |
| Ala Val Asp Ser | Tyr Phe Trp Arg Gln Leu Thr Trp Pro Glu Gly | 230 | 235 | 240 |
| Lys Val Leu Trp | Tyr Asn Thr Val Leu Asn Lys Ser Ser Asn Trp | 245 | 250 | 255 |
| Gly Thr Ser Pro | Leu Leu Trp Tyr Phe Tyr Ser Ala Leu Pro Arg | 260 | 265 | 270 |
| Gly Leu Gly Cys | Ser Leu Leu Phe Ile Pro Leu Gly Leu Val Asp | 275 | 280 | 285 |
| Arg Arg Thr His | Ala Pro Thr Val Leu Ala Leu Gly Phe Met Ala | 290 | 295 | 300 |
| Leu Tyr Ser Leu | Leu Pro His Lys Glu Leu Arg Phe Ile Ile Tyr | 305 | 310 | 315 |
| Ala Phe Pro Met | Leu Asn Ile Thr Ala Ala Arg Gly Cys Ser Tyr | 320 | 325 | 330 |
| Leu Leu Asn Asn | Tyr Lys Lys Ser Trp Leu Tyr Lys Ala Gly Ser | 335 | 340 | 345 |
| Leu Leu Val Ile | Gly His Leu Val Val Asn Ala Ala Tyr Ser Ala | 350 | 355 | 360 |
| Thr Ala Leu Tyr | Val Ser His Phe Asn Tyr Pro Gly Gly Val Ala | 365 | 370 | 375 |
| Met Gln Arg Leu | His Gln Leu Val Pro Pro Gln Thr Asp Val Leu | 380 | 385 | 390 |
| Leu His Ile Asp | Val Ala Ala Ala Gln Thr Gly Val Ser Arg Phe | 395 | 400 | 405 |
| Leu Gln Val Asn | Ser Ala Trp Arg Tyr Asp Lys Arg Glu Asp Val | 410 | 415 | 420 |
| Gln Pro Gly Thr | Gly Met Leu Ala Tyr Thr His Ile Leu Met Glu | 425 | 430 | 435 |
| Ala Ala Pro Gly | Leu Leu Ala Leu Tyr Arg Asp Thr His Arg Val | 440 | 445 | 450 |
| Leu Ala Ser Val | Val Gly Thr Thr Gly Val Ser Leu Asn Leu Thr | 455 | 460 | 465 |
| Gln Leu Pro Pro | Phe Asn Val His Leu Gln Thr Lys Leu Val Leu | 470 | 475 | 480 |
| Leu Glu Arg Leu | Pro Arg Pro Ser                             | 485 |     |     |



<211> 197  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2758485

<400> 53  
 Met Ser Pro Arg Arg Thr Leu Pro Arg Pro Leu Ser Leu Cys Leu  
 1 5 10 15  
 Ser Leu Cys Leu Cys Leu Cys Leu Ala Ala Ala Leu Gly Ser Ala  
 20 25 30  
 Gln Ser Gly Ser Cys Arg Asp Lys Lys Asn Cys Lys Val Val Phe  
 35 40 45  
 Ser Gln Gln Glu Leu Arg Lys Arg Leu Thr Pro Leu Gln Tyr His  
 50 55 60  
 Val Thr Gln Glu Lys Gly Thr Glu Ser Ala Phe Glu Gly Glu Tyr  
 65 70 75  
 Thr His His Lys Asp Pro Gly Ile Tyr Lys Cys Val Val Cys Gly  
 80 85 90  
 Thr Pro Leu Phe Lys Ser Glu Thr Lys Phe Asp Ser Gly Ser Gly  
 95 100 105  
 Trp Pro Ser Phe His Asp Val Ile Asn Ser Glu Ala Ile Thr Phe  
 110 115 120  
 Thr Asp Asp Phe Ser Tyr Gly Met His Arg Val Glu Thr Ser Cys  
 125 130 135  
 Ser Gln Cys Gly Ala His Leu Gly His Ile Phe Asp Asp Gly Pro  
 140 145 150  
 Arg Pro Thr Gly Lys Arg Tyr Cys Ile Asn Ser Ala Ala Leu Ser  
 155 160 165  
 Phe Thr Pro Ala Asp Ser Ser Gly Thr Ala Glu Gly Gly Ser Gly  
 170 175 180  
 Val Ala Ser Pro Ala Gln Ala Asp Lys Ala Asp Ser Glu Ser Asn  
 185 190 195  
 Gly Glu

<210> 54  
 <211> 84  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2763296

<400> 54  
 Met Thr Pro Gln Ser Leu Leu Gln Thr Thr Leu Phe Leu Leu Ser  
 1 5 10 15  
 Leu Leu Phe Leu Val Gln Gly Ala His Gly Arg Gly His Arg Glu  
 20 25 30  
 Asp Phe Arg Phe Cys Ser Gln Arg Asn Gln Thr His Arg Ser Ser  
 35 40 45  
 Leu His Tyr Tyr Trp Ser Met Arg Leu Gln Ala Arg Gly Gly Pro

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          50          55          60
Ser Pro Leu Lys Ser Asn Ser Asp Ser Ala Arg Leu Pro Ile Ser
          65          70          75
Ser Gly Ser Thr Ser Ser Arg Ile
          80

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<210> 55
<211> 97
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte Clone No: 2779436

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<400> 55
Met Gln Leu Gly Thr Gly Leu Leu Leu Ala Ala Val Leu Ser Leu
  1          5          10          15
Gln Leu Ala Ala Ala Glu Ala Ile Trp Cys His Gln Cys Thr Gly
          20          25          30
Phe Gly Gly Cys Ser His Gly Ser Arg Cys Leu Arg Asp Ser Thr
          35          40          45
His Cys Val Thr Thr Ala Thr Arg Val Leu Ser Asn Thr Glu Asp
          50          55          60
Leu Pro Leu Val Thr Lys Met Cys His Ile Gly Cys Pro Asp Ile
          65          70          75
Pro Ser Leu Gly Leu Gly Pro Tyr Val Ser Ile Ala Cys Cys Gln
          80          85          90
Thr Ser Leu Cys Asn His Asp
          95

```

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<210> 56
<211> 140
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte Clone No: 2808528

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```

<400> 56
Met Ala Ala Ser Leu Gly Gln Val Leu Ala Leu Val Leu Val Ala
  1          5          10          15
Ala Leu Trp Gly Gly Thr Gln Pro Leu Leu Lys Arg Ala Ser Ala
          20          25          30
Gly Leu Gln Arg Val His Glu Pro Thr Trp Ala Gln Gln Leu Leu
          35          40          45
Gln Glu Met Lys Thr Leu Phe Leu Asn Thr Glu Tyr Leu Met Pro
          50          55          60
Phe Leu Leu Asn Gln Cys Gly Ser Leu Leu Tyr Tyr Leu Thr Leu
          65          70          75

```

```

Ala Ser Thr Asp Leu Thr Leu Ala Val Pro Ile Cys Asn Ser Leu
      80              85              90
Ala Ile Ile Phe Thr Leu Ile Val Gly Lys Ala Leu Gly Glu Asp
      95              100             105
Ile Gly Gly Lys Arg Ala Val Ala Gly Met Val Leu Thr Val Ile
      110             115             120
Gly Ile Ser Leu Cys Ile Thr Ser Ser Val Ser Lys Thr Gln Gly
      125             130             135
Gln Gln Ser Thr Leu
      140

```

```

<210> 57
<211> 285
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> Incyte Clone No: 2809230

```

```

<400> 57
Met Glu Val Pro Pro Pro Ala Pro Arg Ser Phe Leu Cys Arg Ala
  1              5              10              15
Leu Cys Leu Phe Pro Arg Val Phe Ala Ala Glu Ala Val Thr Ala
      20              25              30
Asp Ser Glu Val Leu Glu Glu Arg Gln Lys Arg Leu Pro Tyr Val
      35              40              45
Pro Glu Pro Tyr Tyr Pro Glu Ser Gly Trp Asp Arg Leu Arg Glu
      50              55              60
Leu Phe Gly Lys Asp Glu Gln Gln Arg Ile Ser Lys Asp Leu Ala
      65              70              75
Asn Ile Cys Lys Thr Ala Ala Thr Ala Gly Ile Ile Gly Trp Val
      80              85              90
Tyr Gly Gly Ile Pro Ala Phe Ile His Ala Lys Gln Gln Tyr Ile
      95              100             105
Glu Gln Ser Gln Ala Glu Ile Tyr His Asn Arg Phe Asp Ala Val
      110             115             120
Gln Ser Ala His Arg Ala Ala Thr Arg Gly Phe Ile Arg Tyr Gly
      125             130             135
Trp Arg Trp Gly Trp Arg Thr Ala Val Phe Val Thr Ile Phe Asn
      140             145             150
Thr Val Asn Thr Ser Leu Asn Val Tyr Arg Asn Lys Asp Ala Leu
      155             160             165
Ser His Phe Val Ile Ala Gly Ala Val Thr Gly Ser Leu Phe Arg
      170             175             180
Ile Asn Val Gly Leu Arg Gly Leu Val Ala Gly Gly Ile Ile Gly
      185             190             195
Ala Leu Leu Gly Thr Pro Val Gly Gly Leu Leu Met Ala Phe Gln
      200             205             210
Lys Tyr Ser Gly Glu Thr Val Gln Glu Arg Lys Gln Lys Asp Arg
      215             220             225
Lys Ala Leu His Glu Leu Lys Leu Glu Glu Trp Lys Gly Arg Leu
      230             235             240
Gln Val Thr Glu His Leu Pro Glu Lys Ile Glu Ser Ser Leu Gln

```

|                 |                     |                     |     |
|-----------------|---------------------|---------------------|-----|
|                 | 245                 | 250                 | 255 |
| Glu Asp Glu Pro | Glu Asn Asp Ala Lys | Lys Ile Glu Ala Leu | Leu |
|                 | 260                 | 265                 | 270 |
| Asn Leu Pro Arg | Asn Pro Ser Val Ile | Asp Lys Gln Asp Lys | Asp |
|                 | 275                 | 280                 | 285 |

&lt;210&gt; 58

&lt;211&gt; 262

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2816821

&lt;400&gt; 58

|                     |                     |                     |
|---------------------|---------------------|---------------------|
| Met Thr Gln Pro Val | Pro Arg Leu Ser Val | Pro Ala Ala Leu Ala |
| 1                   | 5                   | 10                  |
| Leu Gly Ser Ala Ala | Leu Gly Ala Ala Phe | Ala Thr Gly Leu Phe |
|                     | 20                  | 25                  |
| Leu Gly Arg Arg Cys | Pro Pro Trp Arg Gly | Arg Arg Glu Gln Cys |
|                     | 35                  | 40                  |
| Leu Leu Pro Pro Glu | Asp Ser Arg Leu Trp | Gln Tyr Leu Leu Ser |
|                     | 50                  | 55                  |
| Arg Ser Met Arg Glu | His Pro Ala Leu Arg | Ser Leu Arg Leu Leu |
|                     | 65                  | 70                  |
| Thr Leu Glu Gln Pro | Gln Gly Asp Ser Met | Met Thr Cys Glu Gln |
|                     | 80                  | 85                  |
| Ala Gln Leu Leu Ala | Asn Leu Ala Arg Leu | Ile Gln Ala Lys Lys |
|                     | 95                  | 100                 |
| Ala Leu Asp Leu Gly | Thr Phe Thr Gly Tyr | Ser Ala Leu Ala Leu |
|                     | 110                 | 115                 |
| Ala Leu Ala Leu Pro | Ala Asp Gly Arg Val | Val Thr Cys Glu Val |
|                     | 125                 | 130                 |
| Asp Ala Gln Pro Pro | Glu Leu Gly Arg Pro | Leu Trp Arg Gln Ala |
|                     | 140                 | 145                 |
| Glu Ala Glu His Lys | Ile Asp Leu Arg Leu | Lys Pro Ala Leu Glu |
|                     | 155                 | 160                 |
| Thr Leu Asp Glu Leu | Leu Ala Ala Gly Glu | Ala Gly Thr Phe Asp |
|                     | 170                 | 175                 |
| Val Ala Val Val Asp | Ala Asp Lys Glu Asn | Cys Ser Ala Tyr Tyr |
|                     | 185                 | 190                 |
| Glu Arg Cys Leu Gln | Leu Leu Arg Pro Gly | Gly Ile Leu Ala Val |
|                     | 200                 | 205                 |
| Leu Arg Val Leu Trp | Arg Gly Lys Val Leu | Gln Pro Pro Lys Gly |
|                     | 215                 | 220                 |
| Asp Val Ala Ala Glu | Cys Val Arg Asn Leu | Asn Glu Arg Ile Arg |
|                     | 230                 | 235                 |
| Arg Asp Val Arg Val | Tyr Ile Ser Leu Leu | Pro Leu Gly Asp Gly |
|                     | 245                 | 250                 |
| Leu Thr Leu Ala Phe | Lys Ile             |                     |
|                     | 260                 |                     |

<210> 59  
 <211> 189  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2817268

<400> 59  
 Met Ala Leu Leu Ser Arg Pro Ala Leu Thr Leu Leu Leu Leu Leu  
   1                  5                  10                  15  
 Met Ala Ala Val Val Arg Cys Gln Glu Gln Ala Gln Thr Thr Asp  
                   20                  25                  30  
 Trp Arg Ala Thr Leu Lys Thr Ile Arg Asn Gly Val His Lys Ile  
                   35                  40                  45  
 Asp Thr Tyr Leu Asn Ala Ala Leu Asp Leu Leu Gly Gly Glu Asp  
                   50                  55                  60  
 Gly Leu Cys Gln Tyr Lys Cys Ser Asp Gly Ser Lys Pro Phe Pro  
                   65                  70                  75  
 Arg Tyr Gly Tyr Lys Pro Ser Pro Pro Asn Gly Cys Gly Ser Pro  
                   80                  85                  90  
 Leu Phe Gly Val His Leu Asn Ile Gly Ile Pro Ser Leu Thr Lys  
                   95                  100                 105  
 Cys Cys Asn Gln His Asp Arg Cys Tyr Glu Thr Cys Gly Lys Ser  
                  110                 115                 120  
 Lys Asn Asp Cys Asp Glu Glu Phe Gln Tyr Cys Leu Ser Lys Ile  
                  125                 130                 135  
 Cys Arg Asp Val Gln Lys Thr Leu Gly Leu Thr Gln His Val Gln  
                  140                 145                 150  
 Ala Cys Glu Thr Thr Val Glu Leu Leu Phe Asp Ser Val Ile His  
                  155                 160                 165  
 Leu Gly Cys Lys Pro Tyr Leu Asp Ser Gln Arg Ala Ala Cys Arg  
                  170                 175                 180  
 Cys His Tyr Glu Glu Lys Thr Asp Leu  
                  185

<210> 60  
 <211> 257  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2923165

<400> 60  
 Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile Ala Phe Gly  
   1                  5                  10                  15  
 Pro Ala Leu Ala Leu Tyr Val Phe Thr Ile Ala Thr Glu Pro Leu  
                   20                  25                  30  
 Arg Ile Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val Ser  
                   35                  40                  45

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Leu Leu Ile Ser Ser Leu Val Trp Phe Met Ala Arg Val Ile Ile
      50                      55                      60
Asp Asn Lys Asp Gly Pro Thr Gln Lys Tyr Leu Leu Ile Phe Gly
      65                      70                      75
Ala Phe Val Ser Val Tyr Ile Gln Glu Met Phe Arg Phe Ala Tyr
      80                      85                      90
Tyr Lys Leu Leu Lys Lys Ala Ser Glu Gly Leu Lys Ser Ile Asn
      95                      100                     105
Pro Gly Glu Thr Ala Pro Ser Met Arg Leu Leu Ala Tyr Val Ser
     110                     115                     120
Gly Leu Gly Phe Gly Ile Met Ser Gly Val Phe Ser Phe Val Asn
     125                     130                     135
Thr Leu Ser Asp Ser Leu Gly Pro Gly Thr Val Gly Ile His Gly
     140                     145                     150
Asp Ser Pro Gln Phe Phe Leu Tyr Ser Ala Phe Met Thr Leu Val
     155                     160                     165
Ile Ile Leu Leu His Val Phe Trp Gly Ile Val Phe Phe Asp Gly
     170                     175                     180
Cys Glu Lys Lys Lys Trp Gly Ile Leu Leu Ile Val Leu Leu Thr
     185                     190                     195
His Leu Leu Val Ser Ala Gln Thr Phe Ile Ser Ser Tyr Tyr Gly
     200                     205                     210
Ile Asn Leu Ala Ser Ala Phe Ile Ile Leu Val Leu Met Gly Thr
     215                     220                     225
Trp Ala Phe Leu Ala Ala Gly Gly Ser Cys Arg Ser Leu Lys Leu
     230                     235                     240
Cys Leu Leu Cys Gln Asp Lys Asn Phe Leu Leu Tyr Asn Gln Arg
     245                     250                     255
Ser Arg

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&lt;210&gt; 61

&lt;211&gt; 82

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2949822

&lt;400&gt; 61

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Met Pro Phe Ser Trp Met Val Ile Ile Leu Gly Phe Leu Cys Gly
  1          5          10          15
Leu Ser Gly Gln Leu Gln Ile Met Asn Thr Leu Ser Ser Leu Pro
          20          25          30
Ile Val Leu Leu Val Ser Ser Ser Cys Leu Ile Leu Ala Arg Met
          35          40          45
Ser Tyr Ser Ile Leu Thr Ser Ser Tyr Gly Gly Gly Val Phe Ile
          50          55          60
Leu Leu Asp Leu Lys Arg Asn Thr Ser Lys Val Ser Pro Leu Met
          65          70          75
Met Met Phe Ala Ile Gly His
          80

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<210> 62  
 <211> 202  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2992192

<400> 62  
 Met Ala Ala Pro Trp Arg Arg Trp Pro Thr Gly Leu Leu Ala Val  
 1 5 10 15  
 Leu Arg Pro Leu Leu Thr Cys Arg Pro Leu Gln Gly Thr Thr Leu  
 20 25 30  
 Gln Arg Asp Val Leu Leu Phe Glu His Asp Arg Gly Arg Phe Phe  
 35 40 45  
 Thr Ile Leu Gly Leu Phe Cys Ala Gly Gln Gly Val Phe Trp Ala  
 50 55 60  
 Ser Met Ala Val Ala Ala Val Ser Arg Pro Pro Val Pro Val Gln  
 65 70 75  
 Pro Leu Asp Ala Glu Val Pro Asn Arg Gly Pro Phe Asp Leu Arg  
 80 85 90  
 Ser Ala Leu Trp Arg Tyr Gly Leu Ala Val Gly Cys Gly Ala Ile  
 95 100 105  
 Gly Ala Leu Val Leu Gly Ala Gly Leu Leu Phe Ser Leu Arg Ser  
 110 115 120  
 Val Arg Ser Val Val Leu Arg Ala Gly Gly Gln Gln Val Thr Leu  
 125 130 135  
 Thr Thr His Ala Pro Phe Gly Leu Gly Ala His Phe Thr Val Pro  
 140 145 150  
 Leu Lys Gln Val Ser Cys Met Ala His Arg Gly Glu Val Pro Ala  
 155 160 165  
 Met Leu Pro Leu Lys Val Lys Gly Arg Arg Phe Tyr Phe Leu Leu  
 170 175 180  
 Asp Lys Thr Gly His Phe Pro Asn Thr Lys Leu Phe Asp Asn Thr  
 185 190 195  
 Val Gly Ala Tyr Arg Ser Leu  
 200

<210> 63  
 <211> 450  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2992458

<400> 63  
 Met Leu Val Thr Ala Tyr Leu Ala Phe Val Gly Leu Leu Ala Ser  
 1 5 10 15  
 Cys Leu Gly Leu Glu Leu Ser Arg Cys Arg Ala Lys Pro Pro Gly  
 20 25 30

44/167



<210> 64  
 <211> 322  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 3044710

<400> 64  
 Met Ala Arg Cys Phe Ser Leu Val Leu Leu Leu Thr Ser Ile Trp  
 1 5 10 15  
 Thr Thr Arg Leu Leu Val Gln Gly Ser Leu Arg Ala Glu Glu Leu  
 20 25 30  
 Ser Ile Gln Val Ser Cys Arg Ile Met Gly Ile Thr Leu Val Ser  
 35 40 45  
 Lys Lys Ala Asn Gln Gln Leu Asn Phe Thr Glu Ala Lys Glu Ala  
 50 55 60  
 Cys Arg Leu Leu Gly Leu Ser Leu Ala Gly Lys Asp Gln Val Glu  
 65 70 75  
 Thr Ala Leu Lys Ala Ser Phe Glu Thr Cys Ser Tyr Gly Trp Val  
 80 85 90  
 Gly Asp Gly Phe Val Val Ile Ser Arg Ile Ser Pro Asn Pro Lys  
 95 100 105  
 Cys Gly Lys Asn Gly Val Gly Val Leu Ile Trp Lys Val Pro Val  
 110 115 120  
 Ser Arg Gln Phe Ala Ala Tyr Cys Tyr Asn Ser Ser Asp Thr Trp  
 125 130 135  
 Thr Asn Ser Cys Ile Pro Glu Ile Ile Thr Thr Lys Asp Pro Ile  
 140 145 150  
 Phe Asn Thr Gln Thr Ala Thr Gln Thr Thr Glu Phe Ile Val Ser  
 155 160 165  
 Asp Ser Thr Tyr Ser Val Ala Ser Pro Tyr Ser Thr Ile Pro Ala  
 170 175 180  
 Pro Thr Thr Thr Pro Pro Ala Pro Ala Ser Thr Ser Ile Pro Arg  
 185 190 195  
 Arg Lys Lys Leu Ile Cys Val Thr Glu Val Phe Met Glu Thr Ser  
 200 205 210  
 Thr Met Ser Thr Glu Thr Glu Pro Phe Val Glu Asn Lys Ala Ala  
 215 220 225  
 Phe Lys Asn Glu Ala Ala Gly Phe Gly Gly Val Pro Thr Ala Leu  
 230 235 240  
 Leu Val Leu Ala Leu Leu Phe Phe Gly Ala Ala Ala Gly Leu Gly  
 245 250 255  
 Phe Cys Tyr Val Lys Arg Tyr Val Lys Ala Phe Pro Phe Thr Asn  
 260 265 270  
 Lys Asn Gln Gln Lys Glu Met Ile Glu Thr Lys Val Val Lys Glu  
 275 280 285  
 Glu Lys Ala Asn Asp Ser Asn Pro Asn Glu Glu Ser Lys Lys Thr  
 290 295 300  
 Asp Lys Asn Pro Glu Glu Ser Lys Ser Pro Ser Lys Thr Thr Val  
 305 310 315  
 Arg Cys Leu Glu Ala Glu Val  
 320

<210> 65  
 <211> 104  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 3120415

<400> 65  
 Met Lys Leu Ala Ala Leu Leu Gly Leu Cys Val Ala Leu Ser Cys  
     1                    5                    10                    15  
 Ser Ser Ala Ala Ala Phe Leu Val Gly Ser Ala Lys Pro Val Ala  
                     20                    25                    30  
 Gln Pro Val Ala Ala Leu Glu Ser Ala Ala Glu Ala Gly Ala Gly  
                     35                    40                    45  
 Thr Leu Ala Asn Pro Leu Gly Thr Leu Asn Pro Leu Lys Leu Leu  
                     50                    55                    60  
 Leu Ser Ser Leu Gly Ile Pro Val Asn His Leu Ile Glu Gly Ser  
                     65                    70                    75  
 Gln Lys Cys Val Ala Glu Leu Gly Pro Gln Ala Val Gly Ala Val  
                     80                    85                    90  
 Lys Ala Leu Lys Ala Leu Leu Gly Ala Leu Thr Val Phe Gly  
                     95                    100

<210> 66  
 <211> 93  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 126758

<400> 66  
 Met Lys Leu Val Thr Ile Phe Leu Leu Val Thr Ile Ser Leu Cys  
     1                    5                    10                    15  
 Ser Tyr Ser Ala Thr Ala Phe Leu Ile Asn Lys Val Pro Leu Pro  
                     20                    25                    30  
 Val Asp Lys Leu Ala Pro Leu Pro Leu Asp Asn Ile Leu Pro Phe  
                     35                    40                    45  
 Met Asp Pro Leu Lys Leu Leu Leu Lys Thr Leu Gly Ile Ser Val  
                     50                    55                    60  
 Glu His Leu Val Glu Gly Leu Arg Lys Cys Val Asn Glu Leu Gly  
                     65                    70                    75  
 Pro Glu Ala Ser Glu Ala Val Lys Lys Leu Leu Glu Ala Leu Ser  
                     80                    85                    90  
 His Leu Val

<210> 67  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 674760

<400> 67  
 Met Thr Ala Gly Gln Phe Pro Ala Leu Val Ser Leu Ala Leu Leu  
 1 5 10 15  
 Leu Asp Gly Gly Arg Arg Ala Ser Ala Arg Arg Asn Arg Gly His  
 20 25 30  
 Leu Trp Val Phe Cys Thr Ser Phe Leu Leu Ala Pro Trp Glu Val  
 35 40 45  
 Glu Asp Val Gly Trp Lys Lys Gly Leu Asp Leu Pro Pro Ser Ser  
 50 55 60  
 Ser Pro Pro Ser Pro Lys Glu Leu Ala Leu Gln  
 65 70

<210> 68  
 <211> 394  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1229438

<400> 68  
 Met Lys Arg Gln Asn Val Arg Thr Leu Ala Leu Ile Val Cys Thr  
 1 5 10 15  
 Phe Thr Tyr Leu Leu Val Gly Ala Ala Val Phe Asp Ala Leu Glu  
 20 25 30  
 Ser Glu Pro Glu Leu Ile Glu Arg Gln Arg Leu Glu Leu Arg Gln  
 35 40 45  
 Gln Glu Leu Arg Ala Arg Tyr Asn Leu Ser Gln Gly Gly Tyr Glu  
 50 55 60  
 Glu Leu Glu Arg Val Val Leu Arg Leu Lys Pro His Lys Ala Gly  
 65 70 75  
 Val Gln Trp Arg Phe Ala Gly Ser Phe Tyr Phe Ala Ile Thr Val  
 80 85 90  
 Ile Thr Thr Ile Gly Tyr Gly His Ala Ala Pro Ser Thr Asp Gly  
 95 100 105  
 Gly Lys Val Phe Cys Met Phe Tyr Ala Leu Leu Gly Ile Pro Leu  
 110 115 120  
 Thr Leu Val Met Phe Gln Ser Leu Gly Glu Arg Ile Asn Thr Leu  
 125 130 135  
 Val Arg Tyr Leu Leu His Arg Ala Lys Lys Gly Leu Gly Met Arg  
 140 145 150  
 Arg Ala Asp Val Ser Met Ala Asn Met Val Leu Ile Gly Phe Phe  
 155 160 165  
 Ser Cys Ile Ser Thr Leu Cys Ile Gly Ala Ala Ala Phe Ser His

|   |     |     |
|---|-----|-----|
| 170   | 175 | 180 |
| Tyr Glu His Trp Thr Phe Phe Gln Ala Tyr Tyr Tyr Cys Phe Ile |     |     |
| 185   | 190 | 195 |
| Thr Leu Thr Thr Ile Gly Phe Gly Asp Tyr Val Ala Leu Gln Lys |     |     |
| 200   | 205 | 210 |
| Asp Gln Ala Leu Gln Thr Gln Pro Gln Tyr Val Ala Phe Ser Phe |     |     |
| 215   | 220 | 225 |
| Val Tyr Ile Leu Thr Gly Leu Thr Val Ile Gly Ala Phe Leu Asn |     |     |
| 230   | 235 | 240 |
| Leu Val Val Leu Arg Phe Met Thr Met Asn Ala Glu Asp Glu Lys |     |     |
| 245   | 250 | 255 |
| Arg Asp Ala Glu His Arg Ala Leu Leu Thr Arg Asn Gly Gln Ala |     |     |
| 260   | 265 | 270 |
| Gly Gly Gly Gly Gly Gly Gly Ser Ala His Thr Thr Asp Thr Ala |     |     |
| 275   | 280 | 285 |
| Ser Ser Thr Ala Ala Ala Gly Gly Gly Gly Phe Arg Asn Val Tyr |     |     |
| 290   | 295 | 300 |
| Ala Glu Val Leu His Phe Gln Ser Met Cys Ser Cys Leu Trp Tyr |     |     |
| 305   | 310 | 315 |
| Lys Ser Arg Glu Lys Leu Gln Tyr Ser Ile Pro Met Ile Ile Pro |     |     |
| 320   | 325 | 330 |
| Arg Asp Leu Ser Thr Ser Asp Thr Cys Val Glu Gln Ser His Ser |     |     |
| 335   | 340 | 345 |
| Ser Pro Gly Gly Gly Gly Arg Tyr Ser Asp Thr Pro Ser Arg Arg |     |     |
| 350   | 355 | 360 |
| Cys Leu Cys Ser Gly Ala Pro Arg Ser Ala Ile Ser Ser Val Ser |     |     |
| 365   | 370 | 375 |
| Thr Gly Leu His Ser Leu Ser Thr Phe Arg Gly Leu Met Lys Arg |     |     |
| 380   | 385 | 390 |
| Arg Ser Ser Val   |     |     |

&lt;210&gt; 69

&lt;211&gt; 72

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1236935

&lt;400&gt; 69

|   |  |
|---|--|
| Met Cys Pro Phe Phe Pro Leu Thr Ser Leu Ile Val Phe Leu Ile |  |
| 1 5 10 15   |  |
| Leu Phe Phe Lys Thr Ile Ala Ser Ser Gly Ser Gly Gly Ser Cys |  |
| 20 25 30  |  |
| Leu Gly Leu Pro Lys Cys Trp Asp Tyr Arg Arg Glu His Arg Ala |  |
| 35 40 45  |  |
| Arg Pro Thr Ile Val Phe Ser Lys His Val Tyr Thr Tyr Ser Met |  |
| 50 55 60  |  |
| Arg Met Gln Ile Glu Ile Ser Thr Asn Ile Ser Gln             |  |
| 65 70   |  |

<210> 70  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1359283

<400> 70  
 Met Arg Leu Thr Gly Leu Thr Leu Leu Leu Ser Leu Met Glu Ser  
     1                    5                    10                    15  
 Leu Gly Gln Val Glu Asp Arg Phe Phe Ser Thr His Arg Arg Phe  
                     20                    25                    30  
 Pro His His Thr Pro Ile Ser Gly Leu Leu Cys Arg Glu Phe Ser  
                     35                    40                    45  
 Leu Pro Lys Arg Ser Gly Val Pro Trp Thr Arg Val Leu Ile Ser  
                     50                    55                    60  
 Cys Ile Trp Arg Ser Gly Ala Gly Lys Arg Met  
                     65                    70

<210> 71  
 <211> 247  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1450703

<400> 71  
 Met His Leu Ala Arg Leu Val Gly Ser Cys Ser Leu Leu Leu Leu  
     1                    5                    10                    15  
 Leu Gly Ala Leu Ser Gly Trp Ala Ala Ser Asp Asp Pro Ile Glu  
                     20                    25                    30  
 Lys Val Ile Glu Gly Ile Asn Arg Gly Leu Ser Asn Ala Glu Arg  
                     35                    40                    45  
 Glu Val Gly Lys Ala Leu Asp Gly Ile Asn Ser Gly Ile Thr His  
                     50                    55                    60  
 Ala Gly Arg Glu Val Glu Lys Val Phe Asn Gly Leu Ser Asn Met  
                     65                    70                    75  
 Gly Ser His Thr Gly Lys Glu Leu Asp Lys Gly Val Gln Gly Leu  
                     80                    85                    90  
 Asn His Gly Met Asp Lys Val Ala His Glu Ile Asn His Gly Ile  
                     95                    100                    105  
 Gly Gln Ala Gly Lys Glu Ala Glu Lys Leu Gly His Gly Val Asn  
                     110                    115                    120  
 Asn Ala Ala Gly Gln Ala Gly Lys Glu Ala Asp Lys Ala Val Gln  
                     125                    130                    135  
 Gly Phe His Thr Gly Val His Gln Ala Gly Lys Glu Ala Glu Lys  
                     140                    145                    150  
 Leu Gly Gln Gly Val Asn His Ala Ala Asp Gln Ala Gly Lys Glu  
                     155                    160                    165  
 Val Glu Lys Leu Gly Gln Gly Ala His His Ala Ala Gly Gln Ala

|   |     |     |
|---|-----|-----|
| 170   | 175 | 180 |
| Gly Lys Glu Leu Gln Asn Ala His Asn Gly Val Asn Gln Ala Ser |     |     |
| 185   | 190 | 195 |
| Lys Glu Ala Asn Gln Leu Leu Asn Gly Asn His Gln Ser Gly Ser |     |     |
| 200   | 205 | 210 |
| Ser Ser His Gln Gly Gly Ala Thr Thr Thr Pro Leu Ala Ser Gly |     |     |
| 215   | 220 | 225 |
| Ala Ser Val Asn Thr Pro Phe Ile Asn Leu Pro Ala Leu Trp Arg |     |     |
| 230   | 235 | 240 |
| Ser Val Ala Asn Ile Met Pro                                 |     |     |
| 245   |     |     |

&lt;210&gt; 72

&lt;211&gt; 73

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1910668

&lt;400&gt; 72

|   |    |    |
|---|----|----|
| Met Thr Cys Trp Met Leu Pro Pro Ile Ser Phe Leu Ser Tyr Leu |    |    |
| 1   | 5  | 10 |
| Pro Leu Trp Leu Gly Pro Ile Trp Pro Cys Ser Gly Ser Thr Leu |    | 15 |
| 20  | 25 | 30 |
| Gly Lys Pro Asp Pro Gly Val Trp Pro Ser Leu Phe Arg Pro Trp |    |    |
| 35  | 40 | 45 |
| Asp Ala Ala Ser Pro Gly Asn Tyr Ala Leu Ser Arg Gly Glu Asn |    |    |
| 50  | 55 | 60 |
| Gln Tyr Glu Lys Trp Gly Gln Gly Thr His Ser Ser Leu         |    |    |
| 65  | 70 |    |

&lt;210&gt; 73

&lt;211&gt; 70

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1955143

&lt;400&gt; 73

|   |    |    |
|---|----|----|
| Met Gly Arg Leu Arg Tyr Phe Phe Ser Leu Leu Leu Leu Arg Trp |    |    |
| 1   | 5  | 10 |
| Gly Gln Leu Leu Gly Ala Asp Glu Phe Cys Cys His Lys Ser Tyr |    | 15 |
| 20  | 25 | 30 |
| Ile Ala His Leu Val Cys Thr Glu Ser Ala Ile Leu Asn Pro Gly |    |    |
| 35  | 40 | 45 |
| His Ala Leu Glu Leu Tyr Lys Lys Asn Leu Gln Val Ser Ile Leu |    |    |
| 50  | 55 | 60 |

Ser Pro Tyr Pro Thr Asp Pro Ile His Leu  
65 70

<210> 74  
<211> 67  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1961637

<400> 74  
Met Met Phe Thr Ser Leu Ser Leu Ala Leu Pro Phe Leu Leu Gln  
1 5 10 15  
Thr Met Leu Cys Leu Arg Ala Leu Leu Ile Ala Val Pro His Gly  
20 25 30  
His Asp Trp Asn Arg Asp Ala Thr Ser Phe Tyr Thr Ser Thr Val  
35 40 45  
Ser Trp Val Lys Ser Phe Phe Leu Phe Val Leu Asp Gly Val Ser  
50 55 60  
Leu Leu Leu Pro Arg Leu Glu  
65

<210> 75  
<211> 91  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1990762

<400> 75  
Met Trp Pro Thr Thr Trp Ala Trp Ser Trp Val Gln Thr Leu Thr  
1 5 10 15  
Leu Ala Leu Leu Ile Ser Cys Val Thr Leu Gly Gln Leu Ile Thr  
20 25 30  
Thr Leu Gln Val Ser Phe Leu Ile Cys Glu Met Asp Val Ile Ile  
35 40 45  
Gly Cys Asp Glu Met Ile Pro Ser Glu Ser Leu Val Leu Leu Trp  
50 55 60  
Pro Pro Pro Leu Leu Leu Leu Gly Glu Phe Trp Ile Trp Asn Pro  
65 70 75  
Val Ser Arg Ile Leu Phe Trp Leu Cys His Val Pro Ala Gly Gln  
80 85 90  
Leu

<210> 76  
 <211> 56  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1994131

<400> 76  
 Met Asn Glu Trp Trp Leu Leu Leu Leu Leu His Leu His Pro Pro  
   1                  5                  10                  15  
 Arg Val Ile Ser Pro Phe Trp Phe Ile Val Ser Val Leu Thr Ala  
                   20                  25                  30  
 Cys Asp Asn Arg Lys Tyr Ile Leu Leu Arg Thr Val Pro Val Phe  
                   35                  40                  45  
 Ser Phe Pro Glu Asn Thr Tyr Phe Asp Val Gly  
                   50                  55

<210> 77  
 <211> 112  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1997745

<400> 77  
 Met Pro Leu Phe Leu Ser Ile Pro Ser Leu Phe Leu Thr Leu Ser  
   1                  5                  10                  15  
 Gly Leu Gly Leu Ala Val Gln Ser Pro Ala Gly Gly Cys Trp Gly  
                   20                  25                  30  
 Leu Ser Leu Cys Arg His Cys Val Phe Leu Arg Gly Cys Pro Gln  
                   35                  40                  45  
 Asn Thr Pro Pro Ala Pro Trp Gly Ser Ser Gly Ser His Phe Ser  
                   50                  55                  60  
 Trp Ser Leu Arg Ser Gln Lys Gln Leu Leu Gln Glu Ala Lys Lys  
                   65                  70                  75  
 Arg Leu Gly Trp Leu Leu Val Leu Met Met Ala Phe Ile Leu Leu  
                   80                  85                  90  
 Gly His Phe Gly Tyr Ile His Gly His Cys Phe His Leu Ser Phe  
                   95                  100                  105  
 Leu Pro Val Pro Pro Leu Pro  
                   110

<210> 78  
 <211> 54  
 <212> PRT  
 <213> Homo sapiens



<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2009035

<400> 78  
 Met Met Leu Gln Pro Val Asp Leu Leu Gln Ser Tyr Leu Leu Leu  
     1                  5                  10                  15  
 Leu Tyr Cys Trp Ser Phe Ser Leu Leu Phe Thr Leu Leu Cys Asn  
                   20                  25                  30  
 Ala Val Arg Asn Asp Phe Phe His Lys Leu Phe Ser Ile Tyr Trp  
                   35                  40                  45  
 Met Tyr Asn Leu Thr His Ser Lys His  
                   50

<210> 79  
 <211> 57  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2009152

<400> 79  
 Met Lys Phe Tyr Ala Val Leu Leu Ser Ile Cys Leu Leu Leu Ser  
     1                  5                  10                  15  
 Cys Trp Cys Ala Cys His Val Arg Asp Cys Asn Leu Ile Cys Leu  
                   20                  25                  30  
 Phe Ser Thr Val Lys Ala Ile Thr Arg Glu Leu Leu Gln Leu Pro  
                   35                  40                  45  
 Ser Tyr Val Lys Arg Phe Phe Phe Asn Ser Leu Arg  
                   50                  55

<210> 80  
 <211> 52  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2061752

<400> 80  
 Met Gln Arg Leu Gly Lys Ala Pro Gly Thr Trp Gln Ala Ile Ser  
     1                  5                  10                  15  
 Lys Cys Trp Leu Leu Leu Leu Ser Leu Pro Phe Ser Gln Ser  
                   20                  25                  30  
 Ile Ile Ile Ser Leu Arg Ala Gly Thr Met Ser Tyr Leu Pro Leu  
                   35                  40                  45  
 Tyr Phe Pro Gln Tyr Phe Pro  
                   50

<210> 81  
<211> 64  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 2061933

<400> 81  
Met Lys Leu Leu Leu Leu Lys Leu Asp Phe Phe Ile Leu Leu Gly  
1 5 10 15  
Ser Glu Glu Ser Arg Cys Leu Val Asp Val Gln Tyr Val Ile Phe  
20 25 30  
Phe Leu Ile Glu Cys Val His Leu Lys Ser Ser Leu Thr Phe Leu  
35 40 45  
Glu Arg Leu Leu Ser Ile Asn Asn Gly Ile Leu Glu Glu Lys Trp  
50 55 60  
Phe Phe Lys Ser

<210> 82  
<211> 65  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 2081422

<400> 82  
Met Lys Pro Leu Ile Pro Phe Leu Ser Pro Pro Pro Leu Leu Pro  
1 5 10 15  
Leu Thr Phe Phe Leu Ser Ser Leu Leu Leu Ser Pro Leu Cys Arg  
20 25 30  
Ala Leu Gly Thr Ser Gln Ala Val Pro Pro Leu Arg Ala Leu Ser  
35 40 45  
Val Thr Asp Ala His Gly Ser Leu Leu Leu His Pro Lys Thr Leu  
50 55 60  
Ala Cys Pro Cys Leu  
65

<210> 83  
<211> 56  
<212> PRT  
<213> Homo sapiens

<220>  
<221> misc\_feature

<223> Incyte Clone No: 2101278

<400> 83

```

Met Arg Ala Asp Arg Leu Leu Pro Ile Ser Ala Leu Cys Leu Leu
 1             5             10             15
Tyr Thr Pro Gly Gly Ala Leu Glu Pro Ala Gln Val Gly Tyr Thr
             20             25             30
Ile Phe Leu Asn Ser Ile Trp Leu Pro Ala Tyr Phe Phe His Leu
             35             40             45
Phe Thr Val Ile Ser Gly Val Phe Leu Phe Ile
             50             55

```

<210> 84

<211> 120

<212> PRT

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2121353

<400> 84

```

Met Pro Ala Leu Pro Pro Gly Phe Ser Gln Ala Gly Ser Cys Val
 1             5             10             15
Pro Thr Gly Ser Ser Leu Val Leu Cys Leu Leu Ala Ala Ser Leu
             20             25             30
Leu Leu Phe Val Pro Thr Leu Ala Leu Leu Thr Gly Ala Thr Thr
             35             40             45
Cys Trp Cys Leu His Asn Lys Arg Leu Ala Leu Arg Pro Leu Ala
             50             55             60
Trp Gln Gly Leu Trp Gly Leu Val Ser Thr Arg Leu Ser His Gly
             65             70             75
Arg Thr Ser Phe Tyr Phe Asn Ser Leu Pro Leu Gln Thr Asn Ser
             80             85             90
Ser Thr Cys Gln Asn His Ser Trp Asp Ser Gly Ala Arg Ala Thr
             95             100            105
Ala Leu Ala Ser Gly Arg Thr Gln Glu Gly Gly Val Gly Ser Val
             110            115            120

```

<210> 85

<211> 67

<212> PRT

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2241736

<400> 85

```

Met Asn Ser Leu Val Leu Phe Leu Gly His Leu Gly Leu Leu Ile
 1             5             10             15

```

```

Lys Asp Cys Val Leu Leu Phe Ala Met Ser Lys Val Ser Gln Lys
      20                      25                      30
Gln Lys Val Leu Gly Pro Phe Gly Ser Pro Glu Leu Glu Ser Leu
      35                      40                      45
Gly Ile Gly Pro Arg Tyr Leu His Phe His Arg Phe Leu Val Gly
      50                      55                      60
Asp Phe Leu Gln Ala Lys Val
      65

```

```

<210> 86
<211> 62
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 2271935

```

```

<400> 86
Met Ala Trp Leu Ser Phe Ala Ala Val Glu Met Thr Leu Leu Leu
  1          5          10          15
His Ser Ser Ser Leu Leu Ser Phe Ala Lys Val Val Leu Ser Leu
      20          25          30
Pro Glu Ile Arg Pro Phe Gly Asp Gly Asn Phe Ser Leu Lys Gln
      35          40          45
Ser Ser Lys Gln Asn Pro Asn Pro Ala Arg Val Gly Arg Lys Ser
      50          55          60
Met Phe

```

```

<210> 87
<211> 75
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 2295344

```

```

<400> 87
Met Met Ile Leu Leu Ser Leu Leu Val Ala Leu Ile Ser Val Ser
  1          5          10          15
Leu Val Phe Leu Gly Leu Val Arg Phe Ser Arg Glu Asp Phe Ser
      20          25          30
Phe Pro Leu Trp Arg Glu Lys Ala Phe Tyr Gln His Ser Ser Ser
      35          40          45
Ser Val Gly Glu Arg Leu Gln Ala Leu Arg Lys His Ala Phe Thr
      50          55          60
Leu Phe Gly Thr Ile Pro Leu Leu Val Thr Val Pro Gln Val Pro
      65          70          75

```

<210> 88  
 <211> 80  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2303994

<400> 88  
 Met Asn Ser Ile Phe Phe Leu Ser Leu Cys Leu Pro Leu Trp Val  
   1                  5                  10                  15  
 Ser Leu Leu Trp Ala Lys Pro Leu Glu Met His Lys Thr Ser Arg  
                   20                  25                  30  
 His Gly Phe Trp Gln Lys Leu His Asp Phe Lys Leu Ala Leu Leu  
                   35                  40                  45  
 Leu Leu Thr Phe His Arg Glu Lys Ile Phe Pro Leu Lys Lys Thr  
                   50                  55                  60  
 Gly Leu Val Ile Phe Ser Leu Val Ala Leu Ser Arg Asp Ile Ser  
                   65                  70                  75  
 Ala Leu His Tyr Thr  
                   80

<210> 89  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2497805

<400> 89  
 Met Arg Pro Ala Arg Leu Gly Pro Arg Cys Ser Asp Leu Asp Phe  
   1                  5                  10                  15  
 Gly Leu Val Leu Ser Ser Trp Leu Arg Leu Ala Arg Cys Pro Leu  
                   20                  25                  30  
 Glu Ser Ser Phe Gly Phe Ala Phe Phe Val Cys Leu Phe Ser Pro  
                   35                  40                  45  
 Asn Phe Cys Gln Thr  
                   50

<210> 90  
 <211> 116  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2646362

```

<400> 90
Met Trp Trp Ala Leu Cys Ser Met Leu Pro Leu Leu Gly Cys Ala
  1           5           10           15
Cys Ser Ser Gly Cys Trp Gly Ser Gly Pro Thr Pro Leu Leu Ala
           20           25           30
Glu Pro Thr Phe Leu Cys Val Ser Ser Arg Pro His Asn Pro Leu
           35           40           45
Ser Phe Leu Ser Val Leu Pro Cys Ser Arg Gly Pro Gly Pro Ser
           50           55           60
Gly Leu Gln Gly Asp Gly Ala Gly Leu Pro Ala His Leu Gly Pro
           65           70           75
Leu Ser Cys Ile Cys Leu Pro Ser Leu Leu Cys Asp Leu Gly Glu
           80           85           90
Arg Gln Cys Pro Leu Trp Ala Val Arg Ser Thr Gln Cys Leu Ile
           95          100          105
Ala Gly Lys Lys Val Leu Gln Arg Leu Cys Pro
           110          115

```

```

<210> 91
<211> 67
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 2657146

```

```

<400> 91
Met Ile Cys Gln Cys Leu Arg Leu Leu Leu Val Leu Val Thr Leu
  1           5           10           15
Leu Ile Cys Phe Ser Pro Asp Arg Leu Thr Cys Pro Leu Asn Ser
           20           25           30
Ala Val Val Leu Ala Ser Tyr Ala Val Gln Cys Lys Ser Gln Arg
           35           40           45
Glu His Phe Thr Asp Gly Gln Val Val Leu Ile Ser Val Trp Arg
           50           55           60
Lys Ser Leu Val Pro Pro Ala
           65

```

```

<210> 92
<211> 538
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 2755786

```

```

<400> 92
Met Ala Gly Ala Arg Ala Ala Ala Ala Ala Ser Ala Gly Ser
  1           5           10           15

```

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Ala | Ser | Ser | Gly | Asn | Gln | Pro | Pro | Gln | Glu | Leu | Gly | Leu | Gly | 20  | 25  | 30  |
| Glu | Leu | Leu | Glu | Glu | Phe | Ser | Arg | Thr | Gln | Tyr | Arg | Ala | Lys | Asp | 35  | 40  | 45  |
| Gly | Ser | Gly | Thr | Gly | Gly | Ser | Lys | Val | Glu | Arg | Ile | Glu | Lys | Arg | 50  | 55  | 60  |
| Cys | Leu | Glu | Leu | Phe | Gly | Arg | Asp | Tyr | Cys | Phe | Ser | Val | Ile | Pro | 65  | 70  | 75  |
| Asn | Thr | Asn | Gly | Asp | Ile | Cys | Gly | His | Tyr | Pro | Arg | His | Ile | Val | 80  | 85  | 90  |
| Phe | Leu | Glu | Tyr | Glu | Ser | Ser | Glu | Lys | Glu | Lys | Asp | Thr | Phe | Glu | 95  | 100 | 105 |
| Ser | Thr | Val | Gln | Val | Ser | Lys | Leu | Gln | Asp | Leu | Ile | His | Arg | Ser | 110 | 115 | 120 |
| Lys | Met | Ala | Arg | Cys | Arg | Gly | Arg | Phe | Val | Cys | Pro | Val | Ile | Leu | 125 | 130 | 135 |
| Phe | Lys | Gly | Lys | His | Ile | Cys | Arg | Ser | Ala | Thr | Leu | Ala | Gly | Trp | 140 | 145 | 150 |
| Gly | Glu | Leu | Tyr | Gly | Arg | Ser | Gly | Tyr | Asn | Tyr | Phe | Phe | Ser | Gly | 155 | 160 | 165 |
| Gly | Ala | Asp | Asp | Ala | Trp | Ala | Asp | Val | Glu | Asp | Val | Thr | Glu | Glu | 170 | 175 | 180 |
| Asp | Cys | Ala | Leu | Arg | Ser | Gly | Asp | Thr | His | Leu | Phe | Asp | Lys | Val | 185 | 190 | 195 |
| Arg | Gly | Tyr | Asp | Ile | Lys | Leu | Leu | Arg | Tyr | Leu | Ser | Val | Lys | Tyr | 200 | 205 | 210 |
| Ile | Cys | Asp | Leu | Met | Val | Glu | Asn | Lys | Lys | Val | Lys | Phe | Gly | Met | 215 | 220 | 225 |
| Asn | Val | Thr | Ser | Ser | Glu | Lys | Val | Asp | Lys | Ala | Gln | Arg | Tyr | Ala | 230 | 235 | 240 |
| Asp | Phe | Thr | Leu | Leu | Ser | Ile | Pro | Tyr | Pro | Gly | Cys | Glu | Phe | Phe | 245 | 250 | 255 |
| Lys | Glu | Tyr | Lys | Asp | Arg | Asp | Tyr | Met | Ala | Glu | Gly | Leu | Ile | Phe | 260 | 265 | 270 |
| Asn | Trp | Lys | Gln | Asp | Tyr | Val | Asp | Ala | Pro | Leu | Ser | Ile | Pro | Asp | 275 | 280 | 285 |
| Phe | Leu | Thr | His | Ser | Leu | Asn | Ile | Asp | Trp | Ser | Gln | Tyr | Gln | Cys | 290 | 295 | 300 |
| Trp | Asp | Leu | Val | Gln | Gln | Thr | Gln | Asn | Tyr | Leu | Lys | Leu | Leu | Leu | 305 | 310 | 315 |
| Ser | Leu | Val | Asn | Ser | Asp | Asp | Asp | Ser | Gly | Leu | Leu | Val | His | Cys | 320 | 325 | 330 |
| Ile | Ser | Gly | Trp | Asp | Arg | Thr | Pro | Leu | Phe | Ile | Ser | Leu | Leu | Arg | 335 | 340 | 345 |
| Leu | Ser | Leu | Trp | Ala | Asp | Gly | Leu | Ile | His | Thr | Ser | Leu | Lys | Pro | 350 | 355 | 360 |
| Thr | Glu | Ile | Leu | Tyr | Leu | Thr | Val | Ala | Tyr | Asp | Trp | Phe | Leu | Phe | 365 | 370 | 375 |
| Gly | His | Met | Leu | Val | Asp | Arg | Leu | Ser | Lys | Gly | Glu | Glu | Ile | Phe | 380 | 385 | 390 |
| Phe | Phe | Cys | Phe | Asn | Phe | Leu | Lys | His | Ile | Thr | Ser | Glu | Glu | Phe | 395 | 400 | 405 |
| Ser | Ala | Leu | Lys | Thr | Gln | Arg | Arg | Lys | Ser | Leu | Pro | Ala | Arg | Asp | 410 | 415 | 420 |
| Gly | Gly | Phe | Thr | Leu | Glu | Asp | Ile | Cys | Met | Leu | Arg | Arg | Lys | Asp | 425 | 430 | 435 |
| Arg | Gly | Ser | Thr | Thr | Ser | Leu | Gly | Ser | Asp | Phe | Ser | Leu | Val | Met |     |     |     |

|                 |                     |                         |     |  |     |
|-----------------|---------------------|-------------------------|-----|--|-----|
|                 | 440                 |                         | 445 |  | 450 |
| Glu Ser Ser Pro | Gly Ala Thr Gly Ser | Phe Thr Tyr Glu Ala Val |     |  |     |
|                 | 455                 |                         | 460 |  | 465 |
| Glu Leu Val Pro | Ala Gly Ala Pro Thr | Gln Ala Ala Trp Leu Ala |     |  |     |
|                 | 470                 |                         | 475 |  | 480 |
| Ala Leu Ser Asp | Arg Glu Thr Arg Leu | Gln Glu Val Arg Ser Ala |     |  |     |
|                 | 485                 |                         | 490 |  | 495 |
| Phe Leu Ala Ala | Tyr Ser Ser Thr Val | Gly Leu Arg Ala Val Ala |     |  |     |
|                 | 500                 |                         | 505 |  | 510 |
| Pro Ser Pro Ser | Gly Ala Ile Gly Gly | Leu Leu Glu Gln Phe Ala |     |  |     |
|                 | 515                 |                         | 520 |  | 525 |
| Arg Gly Val Gly | Leu Arg Ser Ile Ser | Ser Asn Ala Leu         |     |  |     |
|                 | 530                 |                         | 535 |  |     |

&lt;210&gt; 93

&lt;211&gt; 58

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2831245

&lt;400&gt; 93

|   |  |
|---|--|
| Met Glu Met Lys Gly Ser Arg Val Trp Leu Leu Leu Leu Phe Met |  |
| 1 5 10 15   |  |
| Trp Lys Ala Arg Pro Thr Phe Phe Gln Ser Cys Val Val Pro Phe |  |
| 20 25 30  |  |
| Ile Leu Ser Pro Gln Asn Cys Val Gln Thr His Ser Leu Gly Pro |  |
| 35 40 45  |  |
| Gly Val Trp Leu Gly Val Phe Pro Ser Gly Ser Leu His         |  |
| 50 55   |  |

&lt;210&gt; 94

&lt;211&gt; 119

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 3116250

&lt;400&gt; 94

|   |  |
|---|--|
| Met Lys Val Leu Ile Ser Ser Leu Leu Leu Leu Pro Leu Met     |  |
| 1 5 10 15   |  |
| Leu Met Ser Met Val Ser Ser Ser Leu Asn Pro Gly Val Ala Arg |  |
| 20 25 30  |  |
| Gly His Arg Asp Arg Gly Gln Ala Ser Arg Arg Trp Leu Gln Glu |  |
| 35 40 45  |  |
| Gly Gly Gln Glu Cys Glu Cys Lys Asp Trp Phe Leu Arg Ala Pro |  |
| 50 55 60  |  |



```

Arg Arg Lys Phe Met Thr Val Ser Gly Leu Pro Lys Lys Gln Cys
      65              70              75
Pro Cys Asp His Phe Lys Gly Asn Val Lys Lys Thr Arg His Gln
      80              85              90
Arg His His Arg Lys Pro Asn Lys His Ser Arg Ala Cys Gln Gln
      95              100             105
Phe Leu Lys Gln Cys Gln Leu Arg Ser Phe Ala Leu Pro Leu
      110             115

```

```

<210> 95
<211> 128
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 3129630

```

```

<400> 95
Met Ala Tyr Ser Thr Val Gln Arg Val Ala Leu Ala Ser Gly Leu
  1              5              10              15
Val Leu Ala Leu Ser Leu Leu Leu Pro Lys Ala Phe Leu Ser Arg
      20              25              30
Gly Lys Arg Gln Glu Pro Pro Pro Thr Pro Glu Gly Lys Leu Gly
      35              40              45
Arg Phe Pro Pro Met Met His His His Gln Ala Pro Ser Asp Gly
      50              55              60
Gln Thr Pro Gly Ala Arg Phe Gln Arg Ser His Leu Ala Glu Ala
      65              70              75
Phe Ala Lys Ala Lys Gly Ser Gly Gly Gly Ala Gly Gly Gly Gly
      80              85              90
Ser Gly Arg Gly Leu Met Gly Gln Ile Ile Pro Ile Tyr Gly Phe
      95              100             105
Gly Ile Phe Leu Tyr Ile Leu Tyr Ile Leu Phe Lys Val Ser Arg
      110             115              120
Ile Ile Leu Ile Ile Leu His Gln
      125

```

```

<210> 96
<211> 124
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 007632

```

```

<400> 96
Met Tyr Lys Leu Ala Ser Cys Cys Leu Leu Phe Ile Gly Phe Leu
  1              5              10              15
Asn Pro Leu Leu Ser Leu Pro Leu Leu Asp Ser Arg Glu Ile Ser

```

|     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|
|     | 20  |     | 25  |     | 30  |
| Phe | Gln | Leu | Ser | Ala | Pro |
|     | 35  |     | 40  |     | 45  |
| Glu | Leu | Glu | Arg | Ala | Ser |
|     | 50  |     | 55  |     | 60  |
| Gly | Ala | Glu | Arg | Gly | Asp |
|     | 65  |     | 70  |     | 75  |
| Asn | Ile | Phe | Asn | Pro | Arg |
|     | 80  |     | 85  |     | 90  |
| Ser | Gly | Gln | Asp | Pro | Asn |
|     | 95  |     | 100 |     | 105 |
| Ile | Trp | Lys | Pro | Tyr | Lys |
|     | 110 |     | 115 |     | 120 |
| Lys | Tyr | Cys | Val |     |     |

&lt;210&gt; 97

&lt;211&gt; 182

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1236968

&lt;400&gt; 97

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Trp | Pro | Leu | Ser | Ser | Asp | Ser | Ser | Trp | Ser | Leu | Trp | Ile | Ser |
| 1   |     |     | 5   |     |     |     |     |     | 10  |     |     |     |     | 15  |
| Thr | Gly | Met | Ala | Pro | Ala | Pro | Ser | Ser | Ser | Thr | Arg | Ser | Phe | Ser |
|     |     |     | 20  |     |     |     |     |     | 25  |     |     |     |     | 30  |
| Glu | Ser | Leu | Lys | Gln | Lys | Leu | Val | Arg | Val | Leu | Glu | Glu | Asn | Leu |
|     |     |     | 35  |     |     |     |     |     | 40  |     |     |     |     | 45  |
| Ile | Leu | Ser | Glu | Lys | Ile | Gln | Gln | Leu | Glu | Glu | Gly | Ala | Ala | Ile |
|     |     |     | 50  |     |     |     |     |     | 55  |     |     |     |     | 60  |
| Ser | Ile | Val | Ser | Gly | Gln | Gln | Ser | His | Thr | Tyr | Asp | Asp | Leu | Leu |
|     |     |     | 65  |     |     |     |     |     | 70  |     |     |     |     | 75  |
| His | Lys | Asn | Gln | Gln | Leu | Thr | Met | Gln | Val | Ala | Cys | Leu | Asn | Gln |
|     |     |     | 80  |     |     |     |     |     | 85  |     |     |     |     | 90  |
| Glu | Leu | Ala | Gln | Leu | Lys | Lys | Leu | Glu | Lys | Thr | Val | Ala | Ile | Leu |
|     |     |     | 95  |     |     |     |     |     | 100 |     |     |     |     | 105 |
| His | Glu | Ser | Gln | Arg | Ser | Leu | Val | Val | Thr | Asn | Glu | Tyr | Leu | Leu |
|     |     |     | 110 |     |     |     |     |     | 115 |     |     |     |     | 120 |
| Gln | Gln | Leu | Asn | Lys | Glu | Pro | Lys | Gly | Tyr | Ser | Gly | Lys | Ala | Leu |
|     |     |     | 125 |     |     |     |     |     | 130 |     |     |     |     | 135 |
| Leu | Pro | Pro | Glu | Lys | Gly | His | His | Leu | Gly | Arg | Ser | Ser | Pro | Phe |
|     |     |     | 140 |     |     |     |     |     | 145 |     |     |     |     | 150 |
| Gly | Lys | Ser | Thr | Leu | Ser | Ser | Ser | Ser | Pro | Val | Ala | His | Glu | Thr |
|     |     |     | 155 |     |     |     |     |     | 160 |     |     |     |     | 165 |
| Gly | Gln | Tyr | Leu | Ile | Gln | Ser | Val | Leu | Asp | Ala | Ala | Pro | Glu | Pro |
|     |     |     | 170 |     |     |     |     |     | 175 |     |     |     |     | 180 |
| Gly | Leu |     |     |     |     |     |     |     |     |     |     |     |     |     |

<210> 98  
 <211> 237  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1334153

<400> 98  
 Met Lys Gly Ile Leu Val Ala Gly Ile Thr Ala Val Leu Val Ala  
     1                    5                    10                    15  
 Ala Val Glu Ser Leu Ser Cys Val Pro Cys Asn Ser Trp Glu Lys  
                     20                    25                    30  
 Ser Cys Val Asn Ser Ile Ala Ser Glu Cys Pro Ser His Ala Asn  
                     35                    40                    45  
 Thr Ser Cys Ile Ser Ser Ser Ala Ser Ser Ser Leu Glu Thr Pro  
                     50                    55                    60  
 Val Arg Leu Tyr Gln Asn Met Phe Cys Ser Ala Glu Asn Cys Ser  
                     65                    70                    75  
 Glu Glu Thr His Ile Thr Ala Phe Thr Val His Val Ser Ala Glu  
                     80                    85                    90  
 Glu His Phe His Phe Val Ser Gln Cys Cys Gln Gly Lys Glu Cys  
                     95                    100                    105  
 Ser Asn Thr Ser Asp Ala Leu Asp Pro Pro Leu Lys Asn Val Ser  
                     110                    115                    120  
 Ser Asn Ala Glu Cys Pro Ala Cys Tyr Glu Ser Asn Gly Thr Ser  
                     125                    130                    135  
 Cys Arg Gly Lys Pro Trp Lys Cys Tyr Glu Glu Glu Gln Cys Val  
                     140                    145                    150  
 Phe Leu Val Ala Glu Leu Lys Asn Asp Ile Glu Ser Lys Ser Leu  
                     155                    160                    165  
 Val Leu Lys Gly Cys Ser Asn Val Ser Asn Ala Thr Cys Gln Phe  
                     170                    175                    180  
 Leu Ser Gly Glu Asn Lys Thr Leu Gly Gly Val Ile Phe Arg Lys  
                     185                    190                    195  
 Phe Glu Cys Ala Asn Val Asn Ser Leu Thr Pro Thr Ser Ala Pro  
                     200                    205                    210  
 Thr Thr Ser His Asn Val Gly Ser Lys Ala Ser Leu Tyr Leu Leu  
                     215                    220                    225  
 Ala Leu Ala Ser Leu Leu Leu Arg Gly Leu Leu Pro  
                     230                    235

<210> 99  
 <211> 160  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1396975

<400> 99  
 Met Arg Pro Gly Pro Met Leu Gln Ala Arg Val Ser Ile Pro Ala

```

      1           5           10           15
Ala Leu Gly Thr Leu Phe Pro Arg Pro Gly Trp Ala Pro Gly Glu
      20           25           30
Val Ser Ser Glu Ile Ser Ser Arg Asp Leu Leu Asn Pro His Pro
      35           40           45
Ser Thr Pro Ser Cys Cys Ser Gln Ser Trp Ser Pro Met Ser Val
      50           55           60
Leu Glu Pro Asp Ser Arg Gly Pro Pro Pro Ile Ser Leu Thr His
      65           70           75
Thr Gly Ile His Thr Pro Gln Lys Thr Ser Gln Met Arg Pro Asp
      80           85           90
Ser Gly Ser Arg Gly Met Cys Phe Cys Pro Cys Lys Gly Phe Gly
      95          100          105
Glu Gly Gly Asn Ile Val Glu Ala Gly Lys Ser Pro Gln Thr Cys
      110          115          120
Ala His Ala Pro Pro Ala Leu Arg Phe His Ser Ala Phe Ser Glu
      125          130          135
Cys Pro Cys Cys Thr Gln Thr Thr Gly Gln Glu Arg Pro Ser Leu
      140          145          150
Pro Leu Gln Pro Leu Ser Leu Pro Phe Asn
      155          160

```

&lt;210&gt; 100

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1501749

&lt;400&gt; 100

```

Met Ala Ala Ser Pro Ala Arg Pro Ala Val Leu Ala Leu Thr Gly
      1           5           10           15
Leu Ala Leu Leu Leu Leu Leu Cys Trp Gly Pro Gly Gly Ile Ser
      20           25           30
Gly Asn Lys Leu Lys Leu Met Leu Gln Lys Arg Glu Ala Pro Val
      35           40           45
Pro Thr Lys Thr Lys Val Ala Val Asp Glu Asn Lys Ala Lys Glu
      50           55           60
Phe Leu Gly Ser Leu Lys Arg Gln Lys Arg Gln Leu Trp Asp Arg
      65           70           75
Thr Arg Pro Glu Val Gln Gln Trp Tyr Gln Gln Phe Leu Tyr Met
      80           85           90
Gly Phe Asp Glu Ala Lys Phe Glu Asp Asp Ile Thr Tyr Trp Leu
      95          100          105
Asn Arg Asp Arg Asn Gly His Glu Tyr Tyr Gly Asp Tyr Tyr Gln
      110          115          120
Arg His Tyr Asp Glu Asp Ser Ala Ile Gly Pro Arg Ser Pro Tyr
      125          130          135
Gly Phe Arg His Gly Ala Ser Val Asn Tyr Asp Asp Tyr
      140          145

```

<210> 101  
 <211> 170  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1575240

<400> 101  
 Met Thr Pro Thr Lys Arg Glu Pro Pro Ala Ala Pro Leu Leu Leu  
 1 5 10 15  
 Arg Val Leu Pro Gln Leu Ser Ala Met Ser Leu Arg Leu Ser Thr  
 20 25 30  
 Arg Arg Glu Asp Met Ile Gly Gln Thr Ser Gly Met Cys Ser Phe  
 35 40 45  
 Cys Ser Phe Gln Asn Met Arg Gly Glu Ser Ile Trp Leu Leu Cys  
 50 55 60  
 Leu Glu Glu Glu Gly Ala Gly Leu Cys Gln Asn Ser Leu Asp Lys  
 65 70 75  
 Arg Phe Ser Gln Lys Glu Gly Cys Ser Asp Asp Lys Ser Pro Leu  
 80 85 90  
 His His Phe Pro Trp Leu Ser Asp Ala Pro Pro Ser Ser His Ala  
 95 100 105  
 Arg Thr Ser Glu Ile Arg Leu Pro Pro Asp Ile Thr Gln Pro Cys  
 110 115 120  
 Leu Thr Lys Arg Gln Trp Phe Ile Pro Ser Leu Gly Glu Lys Arg  
 125 130 135  
 Gly Asn Ala Lys Leu Leu His Gln Leu Leu Ile Leu Leu Pro Ala  
 140 145 150  
 Arg Asn Pro Gly Tyr Leu Gln Val Ser Leu Pro Leu Val Trp Ser  
 155 160 165  
 Trp Leu Ser Leu Phe  
 170

<210> 102  
 <211> 150  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1647884

<400> 102  
 Met Gly Ala Ala Ala Trp Ala Arg Pro Leu Ser Val Ser Phe Leu  
 1 5 10 15  
 Leu Leu Leu Leu Pro Leu Pro Gly Met Pro Ala Gly Ser Trp Asp  
 20 25 30  
 Pro Ala Gly Tyr Leu Leu Tyr Cys Pro Cys Met Gly Lys Ala Ser  
 35 40 45  
 Gln Ala Leu Cys Ser Asp Gly Glu Thr Glu Ala Gly Arg Gly Lys  
 50 55 60

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Thr | Pro | Gln | Met | Arg | Pro | Glu | Thr | Pro | Ser | Gln | Val | Gln | Glu |
|     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |
| Arg | Thr | Ser | Glu | Arg | Asp | Gly | Ala | Cys | Ser | Ser | Pro | Leu | Cys | Leu |
|     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |
| Ser | Cys | Lys | Gly | Thr | Glu | Gly | Pro | Thr | Cys | Pro | Thr | Phe | His | Leu |
|     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |
| Thr | Asp | Glu | Lys | Thr | Glu | Ala | Gly | Arg | Gly | Tyr | Val | Thr | Cys | Leu |
|     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |
| Arg | Ser | Lys | Pro | Val | Gln | Gly | Pro | Val | Asn | Gly | Val | Ser | Gly | Ala |
|     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |
| Gly | Leu | Asp | Val | Thr | Asp | Pro | Arg | Trp | Leu | Leu | Val | Ile | Phe | His |
|     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |

&lt;210&gt; 103

&lt;211&gt; 142

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1661144

&lt;400&gt; 103

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Gly | Cys | Leu | Val | Trp | Gly | Pro | Ser | Trp | Pro | Pro | Leu | Ser | Leu |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |
| Leu | Ala | Ser | Leu | Leu | His | Ser | Gly | Ile | Ala | Gly | Arg | Cys | Leu | Leu |
|     |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |
| Cys | Leu | Phe | Lys | Gly | Leu | Ala | Ala | Ala | Ala | Ser | Leu | Gln | Ile | Arg |
|     |     |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |
| Asp | Leu | Ala | Ser | Arg | Leu | Thr | Thr | Gly | Pro | Arg | Thr | Cys | Arg | Val |
|     |     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |
| Gln | Pro | Pro | Pro | His | Pro | Gln | Ser | Ser | Pro | Pro | Trp | Pro | Gly | Pro |
|     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |
| Pro | Gly | Ala | Glu | Thr | Cys | Arg | Pro | Leu | Ser | Arg | Thr | Val | Gly | Gly |
|     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |
| Val | Cys | Pro | Ser | Asp | Trp | Pro | Val | Ser | Trp | Leu | Leu | Leu | Pro | Pro |
|     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |
| Leu | Pro | Glu | Val | Val | Thr | Cys | Ser | Cys | Pro | Arg | Ile | Lys | Ala | Arg |
|     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |
| Pro | Glu | Arg | Thr | Pro | Glu | Leu | Leu | Cys | Ala | Trp | Gly | Gly | Arg | Gly |
|     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |
| Lys | His | Ser | Gln | Leu | Val | Ala |     |     |     |     |     |     |     |     |
|     |     |     |     | 140 |     |     |     |     |     |     |     |     |     |     |

&lt;210&gt; 104

&lt;211&gt; 110

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

<223> Incyte Clone No: 1685409

<400> 104

```

Met Glu Thr Gly Arg Leu Leu Ser Leu Ser Ser Leu Pro Leu Val
  1              5              10              15
Leu Leu Gly Trp Glu Tyr Ser Ser Gln Thr Leu Asn Leu Val Pro
              20              25              30
Ser Thr Ser Ile Leu Ser Phe Val Pro Phe Ile Pro Leu His Leu
              35              40              45
Val Leu Phe Ala Leu Trp Tyr Leu Pro Val Pro His His Leu Tyr
              50              55              60
Pro Gln Gly Leu Gly Asp His Ala Ala Glu Ala Glu Lys Gly Lys
              65              70              75
Arg Glu Glu Gly Gly Thr Gln Val Ala Leu Trp Leu Arg Val Gln
              80              85              90
Pro Ser Cys Pro Ser Pro Val Cys Leu Glu Pro Val Pro Pro Arg
              95              100             105
Ser Arg Phe Leu Leu
              110

```

<210> 105

<211> 120

<212> PRT

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1731419

<400> 105

```

Met Ser Arg Ala Gly Met Leu Gly Val Val Cys Ala Leu Leu Val
  1              5              10              15
Trp Ala Tyr Leu Ala Val Gly Lys Leu Val Val Arg Met Thr Phe
              20              25              30
Thr Glu Leu Cys Thr His His Pro Trp Ser Leu Arg Cys Glu Ser
              35              40              45
Phe Cys Arg Ser Arg Val Thr Ala Cys Leu Pro Ala Pro Ala Pro
              50              55              60
Trp Leu Arg Pro Phe Leu Cys Pro Met Leu Phe Ser Asp Arg Asn
              65              70              75
Pro Val Glu Cys His Leu Phe Gly Glu Ala Val Ser Asp Pro Val
              80              85              90
Cys Lys Gly Leu Leu Pro His Tyr Phe Trp His Pro Thr Phe Phe
              95              100             105
Pro Val Lys Ala Asn Cys Leu Val Ser Phe Cys Pro Thr Thr Val
              110              115             120

```

<210> 106

<211> 135

<212> PRT

<213> Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2650265

&lt;400&gt; 106

```

Met Ala Arg Phe Trp Val Cys Val Ala Gly Ala Gly Phe Phe Leu
 1           5           10           15
Ala Phe Leu Val Leu His Ser Arg Phe Cys Gly Ser Pro Val Leu
          20           25           30
Arg Asn Phe Thr Phe Ala Val Ser Trp Arg Thr Glu Lys Ile Leu
          35           40           45
Tyr Arg Leu Asp Val Gly Trp Pro Lys His Pro Glu Tyr Phe Thr
          50           55           60
Gly Thr Thr Phe Cys Val Ala Val Asp Ser Leu Asn Gly Leu Val
          65           70           75
Tyr Ile Gly Gln Arg Gly Asp Asn Ile Pro Lys Ile Leu Val Phe
          80           85           90
Thr Glu Asp Gly Tyr Phe Leu Arg Ala Trp Asn Tyr Thr Val Asp
          95          100          105
Thr Pro His Gly Ile Phe Ala Ala Ser Thr Leu Tyr Glu Gln Ser
          110          115          120
Val Trp Ile Thr Asp Val Gly Ser Gly Met Tyr Ser Asn Ile Tyr
          125          130          135

```

&lt;210&gt; 107

&lt;211&gt; 301

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2677129

&lt;400&gt; 107

```

Met Leu Met Ile Ile Ile Ile Glu Pro Phe Ser Val Leu Ile Leu
 1           5           10           15
Phe Lys Ser Gly Ile Leu Ala Asp Phe Phe Ala Leu Leu Leu Leu
          20           25           30
Ile Asn Phe Phe Leu Val Ser Phe Phe Leu Ala Tyr Pro Leu Phe
          35           40           45
Asn Asn Gln Ile Asn Ser Arg Ser Met Asn Glu Ile Lys Asn Leu
          50           55           60
Gln Tyr Leu Pro Arg Thr Ser Glu Pro Arg Glu Val Leu Phe Glu
          65           70           75
Asp Arg Thr Arg Ala His Ala Asp His Val Gly Gln Gly Phe Asp
          80           85           90
Trp Gln Ser Thr Ala Ala Val Gly Val Leu Lys Ala Val Gln Phe
          95          100          105
Gly Glu Trp Ser Asp Gln Pro Arg Ile Thr Lys Asp Val Ile Cys
          110          115          120
Phe His Ala Glu Asp Phe Thr Asp Val Val Gln Arg Leu Gln Leu
          125          130          135
Asp Leu His Glu Pro Pro Val Ser Gln Cys Val Gln Trp Val Asp
          140          145          150

```



```

Glu Ala Lys Leu Asn Gln Met Arg Arg Glu Gly Ile Arg Tyr Ala
      155      160      165
Arg Ile Gln Leu Cys Asp Asn Asp Ile Tyr Phe Ile Pro Arg Asn
      170      175      180
Val Ile His Gln Phe Lys Thr Val Ser Ala Val Cys Ser Leu Ala
      185      190      195
Trp His Ile Arg Leu Lys Gln Tyr His Pro Val Val Glu Ala Thr
      200      205      210
Gln Asn Thr Glu Ser Asn Ser Asn Met Asp Cys Gly Leu Thr Gly
      215      220      225
Lys Arg Glu Leu Glu Val Asp Ser Gln Cys Val Arg Ile Lys Thr
      230      235      240
Glu Ser Glu Glu Ala Cys Thr Glu Ile Gln Leu Leu Thr Thr Ala
      245      250      255
Ser Ser Ser Phe Pro Pro Ala Ser Glu Leu Asn Leu Gln Gln Asp
      260      265      270
Gln Lys Thr Gln Pro Ile Pro Val Leu Lys Val Glu Ser Arg Leu
      275      280      285
Asp Ser Asp Gln Gln His Asn Leu Gln Glu His Ser Thr Thr Ser
      290      295      300
Val

```

&lt;210&gt; 108

&lt;211&gt; 103

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 3151073

&lt;400&gt; 108

```

Met Ser Phe Val Pro Gly Leu Leu Leu Cys Phe Val Leu Leu Leu
  1      5      10      15
Cys Val Ser Pro Val Tyr Leu Pro Ser Arg Ser Pro Ser Thr Phe
      20      25      30
Pro Ile Ser Glu Pro Leu Ser Phe Ile Gly Met Ser Ala Trp Pro
      35      40      45
Gln Cys Ser Pro Ile Tyr Ser Gln Thr Pro Gly Leu Ala Tyr Glu
      50      55      60
Pro Ser Ser Phe Pro Lys Arg Arg Tyr Trp Val Cys Thr Leu His
      65      70      75
Glu Ile Lys Trp Glu Cys Pro Arg Ser Arg Arg Thr Ser Asp Ala
      80      85      90
Val His Ala Asn Lys Leu Gly Leu Pro Leu Lys Ile Ile
      95      100

```

&lt;210&gt; 109

&lt;211&gt; 95

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 3170095

&lt;400&gt; 109

```

Met Lys Phe Leu Leu Leu Val Leu Ala Ala Leu Gly Phe Leu Thr
 1           5           10           15
Gln Val Ile Pro Ala Ser Ala Gly Gly Ser Lys Cys Val Ser Asn
           20           25           30
Thr Pro Gly Tyr Cys Arg Thr Cys Cys His Trp Gly Glu Thr Ala
           35           40           45
Leu Phe Met Cys Asn Ala Ser Arg Lys Cys Cys Ile Ser Tyr Ser
           50           55           60
Phe Leu Pro Lys Pro Asp Leu Pro Gln Leu Ile Gly Asn His Trp
           65           70           75
Gln Ser Arg Arg Arg Asn Thr Gln Arg Lys Asp Lys Lys Gln Gln
           80           85           90
Thr Thr Val Thr Ser
           95

```

&lt;210&gt; 110

&lt;211&gt; 113

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 3475168

&lt;400&gt; 110

```

Met Ser Pro Ser Pro Arg Trp Gly Phe Leu Cys Val Leu Phe Thr
 1           5           10           15
Ala Val His Pro Ala Pro Ser Thr Ala Pro Val Gln Asp Lys Cys
           20           25           30
Pro Val Asn Thr Trp Glu Ala Met Gln Ala Ser Ser Gln Gln Leu
           35           40           45
Leu Gln Thr Asp Pro Arg Pro Lys Pro Phe Leu Leu Pro Pro Leu
           50           55           60
Pro Pro Leu Leu Leu Ile Ser Ala Gly Thr Glu Val Ser Ser Leu
           65           70           75
Val Phe Gln Lys Ser Pro Leu His Thr Gln Pro Glu Gly Ala Ile
           80           85           90
Lys Thr Ala Gly Gln Pro Thr Ser Val His Ser Lys Val Leu Ser
           95          100          105
Lys Gly Ser Leu Leu Leu Gly Glu
           110

```

&lt;210&gt; 111

&lt;211&gt; 234

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 3836893

&lt;400&gt; 111

```

Met Arg Lys Thr Arg Leu Trp Gly Leu Leu Trp Met Leu Phe Val
 1           5           10           15
Ser Glu Leu Arg Ala Ala Thr Lys Leu Thr Glu Glu Lys Tyr Glu
 20           25           30
Leu Lys Glu Gly Gln Thr Leu Asp Val Lys Cys Asp Tyr Thr Leu
 35           40           45
Glu Lys Phe Ala Ser Ser Gln Lys Ala Trp Gln Ile Ile Arg Asp
 50           55           60
Gly Glu Met Pro Lys Thr Leu Ala Cys Thr Glu Arg Pro Ser Lys
 65           70           75
Asn Ser His Pro Val Gln Val Gly Arg Ile Ile Leu Glu Asp Tyr
 80           85           90
His Asp His Gly Leu Leu Arg Val Arg Met Val Asn Leu Gln Val
 95          100          105
Glu Asp Ser Gly Leu Tyr Gln Cys Val Ile Tyr Gln Pro Pro Lys
110          115          120
Glu Pro His Met Leu Phe Asp Arg Ile Arg Leu Val Val Thr Lys
125          130          135
Gly Phe Ser Gly Thr Pro Gly Ser Asn Glu Asn Ser Thr Gln Asn
140          145          150
Val Tyr Lys Ile Pro Pro Thr Thr Thr Lys Ala Leu Cys Pro Leu
155          160          165
Tyr Thr Ser Pro Arg Thr Val Thr Gln Ala Pro Pro Lys Ser Thr
170          175          180
Ala Asp Val Ser Thr Pro Asp Ser Glu Ile Asn Leu Thr Asn Val
185          190          195
Thr Asp Ile Ile Arg Val Pro Val Phe Asn Ile Val Ile Leu Leu
200          205          210
Ala Gly Gly Phe Leu Ser Lys Ser Leu Val Phe Ser Val Leu Phe
215          220          225
Ala Val Thr Leu Arg Ser Phe Val Pro
230

```

&lt;210&gt; 112

&lt;211&gt; 119

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 4072159

&lt;400&gt; 112

```

Met Val Leu Pro Leu Pro Trp Leu Ser Arg Tyr His Phe Leu Arg
 1           5           10           15
Leu Leu Leu Pro Ser Trp Ser Leu Ala Pro Gln Gly Ser His Gly
 20           25           30
Cys Cys Ser Gln Asn Pro Lys Ala Ser Met Glu Glu Gln Thr Asn
 35           40           45

```

```

Ser Arg Gly Asn Gly Lys Met Thr Ser Pro Pro Arg Gly Pro Gly
      50                      55                      60
Thr His Arg Thr Ala Glu Leu Ala Arg Ala Glu Glu Leu Leu Glu
      65                      70                      75
Gln Gln Leu Glu Leu Tyr Gln Ala Leu Leu Glu Gly Gln Glu Gly
      80                      85                      90
Ala Trp Glu Ala Gln Ala Leu Val Leu Lys Ile Gln Lys Leu Lys
      95                      100                     105
Glu Gln Met Arg Arg His Gln Glu Ser Leu Gly Gly Gly Ala
      110                     115

```

```

<210> 113
<211> 200
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 1003916

```

```

<400> 113
Met Ala Ser Ser Leu Thr Cys Thr Gly Val Ile Trp Ala Leu Leu
  1      5      10      15
Ser Phe Leu Cys Ala Ala Thr Ser Cys Val Gly Phe Phe Met Pro
      20      25      30
Tyr Trp Leu Trp Gly Ser Gln Leu Gly Lys Pro Val Ser Phe Gly
      35      40      45
Thr Phe Arg Arg Cys Ser Tyr Pro Val His Asp Glu Ser Arg Gln
      50      55      60
Met Met Val Met Val Glu Glu Cys Gly Arg Tyr Ala Ser Phe Gln
      65      70      75
Gly Ile Pro Ser Ala Glu Trp Arg Ile Cys Thr Ile Val Thr Gly
      80      85      90
Leu Gly Cys Gly Leu Leu Leu Leu Val Ala Leu Thr Ala Leu Met
      95     100     105
Gly Cys Cys Val Ser Asp Leu Ile Ser Arg Thr Val Gly Arg Val
      110     115     120
Ala Gly Gly Ile Gln Phe Leu Gly Gly Leu Leu Ile Gly Ala Gly
      125     130     135
Cys Ala Leu Tyr Pro Leu Gly Trp Asp Ser Glu Glu Val Arg Gln
      140     145     150
Thr Cys Gly Tyr Thr Ser Gly Gln Phe Asp Leu Gly Lys Cys Glu
      155     160     165
Ile Gly Trp Ala Tyr Tyr Cys Thr Gly Ala Gly Ala Thr Ala Ala
      170     175     180
Met Leu Leu Cys Thr Trp Leu Ala Cys Phe Ser Gly Lys Lys Gln
      185     190     195
Lys His Tyr Pro Tyr
      200

```

```

<210> 114

```

<211> 225  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2093492

<400> 114  
 Met Gly Phe Arg Leu Glu Gly Ile Phe Pro Ala Ala Leu Leu Pro  
 1 5 10 15  
 Leu Leu Leu Thr Met Ile Leu Phe Leu Gly Pro Leu Met Gln Leu  
 20 25 30  
 Ser Met Asp Cys Pro Cys Asp Leu Ala Asp Gly Leu Lys Val Val  
 35 40 45  
 Leu Ala Pro Arg Ser Trp Ala Arg Cys Leu Thr Asp Met Arg Trp  
 50 55 60  
 Leu Arg Asn Gln Val Ile Ala Pro Leu Thr Glu Glu Leu Val Phe  
 65 70 75  
 Arg Ala Cys Met Leu Pro Met Leu Ala Pro Cys Met Gly Leu Gly  
 80 85 90  
 Pro Ala Val Phe Thr Cys Pro Leu Phe Phe Gly Val Ala His Phe  
 95 100 105  
 His His Ile Ile Glu Gln Leu Arg Phe Arg Gln Ser Ser Val Gly  
 110 115 120  
 Asn Ile Phe Leu Ser Ala Ala Phe Gln Phe Ser Tyr Thr Ala Val  
 125 130 135  
 Phe Gly Ala Tyr Thr Ala Phe Leu Phe Ile Arg Thr Gly His Leu  
 140 145 150  
 Ile Gly Pro Val Leu Cys His Ser Phe Cys Asn Tyr Met Gly Phe  
 155 160 165  
 Pro Ala Val Cys Ala Ala Leu Glu His Pro Gln Arg Arg Pro Leu  
 170 175 180  
 Leu Ala Gly Tyr Ala Leu Gly Val Gly Leu Phe Leu Leu Leu Leu  
 185 190 195  
 Gln Pro Leu Thr Asp Pro Lys Leu Tyr Gly Ser Leu Pro Leu Cys  
 200 205 210  
 Val Leu Leu Glu Arg Ala Gly Asp Ser Glu Ala Pro Leu Cys Ser  
 215 220 225

<210> 115  
 <211> 155  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2108789

<400> 115  
 Met Ser Gly Leu Leu Ile Pro Pro Leu Pro Gly Trp Val Leu Gly  
 1 5 10 15  
 Pro Leu Met Trp Ala Cys Arg Pro Pro Gln Asp Glu Pro Ser Gly  
 20 25 30

```

Thr Asp Pro Pro Pro Pro Arg Leu Gln Pro His His Val Ser Gly
      35                      40                      45
Leu Gly Leu Gly Gln Ala Trp Ala Gln Ser Trp Ala Pro Arg Gly
      50                      55                      60
Ser Pro Pro Leu Thr Trp Leu Leu Pro Thr Leu Pro Leu Lys Asp
      65                      70                      75
Gly Pro Ala Ala Arg Leu Pro Pro Pro Pro His Thr Thr Leu Gly
      80                      85                      90
Gly Leu Ser His Pro Pro Gln Pro Arg Ser Ala Gln Thr Asp Pro
      95                      100                     105
His Ser Ile Pro Arg Pro Ala Ala Gln Val Arg Gly Pro Val Leu
     110                      115                     120
Pro Gly Ala Trp Ala Thr Pro Tyr Ala Ile Ser Ser Glu Gln Pro
     125                      130                     135
Gly Pro Thr Asp Pro His Ala Leu Ser Tyr Val Pro Phe Ser Pro
     140                      145                     150
Asp Phe Phe Cys Thr
      155

```

&lt;210&gt; 116

&lt;211&gt; 468

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2171401

&lt;400&gt; 116

```

Met Gly Arg Gly Trp Gly Phe Leu Phe Gly Leu Leu Gly Ala Val
  1           5           10           15
Trp Leu Leu Ser Ser Gly His Gly Glu Glu Gln Pro Pro Glu Thr
  20           25           30
Ala Ala Gln Arg Cys Phe Cys Gln Val Ser Gly Tyr Leu Asp Asp
  35           40           45
Cys Thr Cys Asp Val Glu Thr Ile Asp Arg Phe Asn Asn Tyr Arg
  50           55           60
Leu Phe Pro Arg Leu Gln Lys Leu Leu Glu Ser Asp Tyr Phe Arg
  65           70           75
Tyr Tyr Lys Val Asn Leu Lys Arg Pro Cys Pro Phe Trp Asn Asp
  80           85           90
Ile Ser Gln Cys Gly Arg Arg Asp Cys Ala Val Lys Pro Cys Gln
  95           100          105
Ser Asp Glu Val Pro Asp Gly Ile Lys Ser Ala Ser Tyr Lys Tyr
  110          115          120
Ser Glu Glu Ala Asn Asn Leu Ile Glu Glu Cys Glu Gln Ala Glu
  125          130          135
Arg Leu Gly Ala Val Asp Glu Ser Leu Ser Glu Glu Thr Gln Lys
  140          145          150
Ala Val Leu Gln Trp Thr Lys His Asp Asp Ser Ser Asp Asn Phe
  155          160          165
Cys Glu Ala Asp Asp Ile Gln Ser Pro Glu Ala Glu Tyr Val Asp
  170          175          180
Leu Leu Leu Asn Pro Glu Arg Tyr Thr Gly Tyr Lys Gly Pro Asp

```

|   |     |     |
|---|-----|-----|
| 185   | 190 | 195 |
| Ala Trp Lys Ile Trp Asn Val Ile Tyr Glu Glu Asn Cys Phe Lys |     |     |
| 200   | 205 | 210 |
| Pro Gln Thr Ile Lys Arg Pro Leu Asn Pro Leu Ala Ser Gly Gln |     |     |
| 215   | 220 | 225 |
| Gly Thr Ser Glu Glu Asn Thr Phe Tyr Ser Trp Leu Glu Gly Leu |     |     |
| 230   | 235 | 240 |
| Cys Val Glu Lys Arg Ala Phe Tyr Arg Leu Ile Ser Gly Leu His |     |     |
| 245   | 250 | 255 |
| Ala Ser Ile Asn Val His Leu Ser Ala Arg Tyr Leu Leu Gln Glu |     |     |
| 260   | 265 | 270 |
| Thr Trp Leu Glu Lys Lys Trp Gly His Asn Ile Thr Glu Phe Gln |     |     |
| 275   | 280 | 285 |
| Gln Arg Phe Asp Gly Ile Leu Thr Glu Gly Glu Gly Pro Arg Arg |     |     |
| 290   | 295 | 300 |
| Leu Lys Asn Leu Tyr Phe Leu Tyr Leu Ile Glu Leu Arg Ala Leu |     |     |
| 305   | 310 | 315 |
| Ser Lys Val Leu Pro Phe Phe Glu Arg Pro Asp Phe Gln Leu Phe |     |     |
| 320   | 325 | 330 |
| Thr Gly Asn Lys Ile Gln Asp Glu Glu Asn Lys Met Leu Leu Leu |     |     |
| 335   | 340 | 345 |
| Glu Ile Leu His Glu Ile Lys Ser Phe Pro Leu His Phe Asp Glu |     |     |
| 350   | 355 | 360 |
| Asn Ser Phe Phe Ala Gly Asp Lys Lys Glu Ala His Lys Leu Lys |     |     |
| 365   | 370 | 375 |
| Glu Asp Phe Arg Leu His Phe Arg Asn Ile Ser Arg Ile Met Asp |     |     |
| 380   | 385 | 390 |
| Cys Val Gly Cys Phe Lys Cys Arg Leu Trp Gly Lys Leu Gln Thr |     |     |
| 395   | 400 | 405 |
| Gln Gly Leu Gly Thr Ala Leu Lys Ile Leu Phe Ser Glu Lys Leu |     |     |
| 410   | 415 | 420 |
| Ile Ala Asn Met Pro Glu Ser Gly Pro Ser Tyr Glu Phe His Leu |     |     |
| 425   | 430 | 435 |
| Thr Arg Gln Glu Ile Val Ser Leu Phe Asn Ala Phe Gly Arg Ile |     |     |
| 440   | 445 | 450 |
| Ser Thr Ser Val Lys Glu Leu Glu Asn Phe Arg Asn Leu Leu Gln |     |     |
| 455   | 460 | 465 |
| Asn Ile His   |     |     |

&lt;210&gt; 117

&lt;211&gt; 403

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2212530

&lt;400&gt; 117

|   |
|---|
| Met Ser Thr Ser Thr Ser Pro Ala Ala Met Leu Leu Arg Arg Leu |
| 1 5 10 15   |
| Arg Arg Leu Ser Trp Gly Ser Thr Ala Val Gln Leu Phe Ile Leu |
| 20 25 30  |
| Thr Val Val Thr Phe Gly Leu Leu Ala Pro Leu Ala Cys His Arg |

|                                     |                         |     |
|-------------------------------------|-------------------------|-----|
| 35                                  | 40                      | 45  |
| Leu Leu His Ser Tyr Phe Tyr Leu Arg | His Trp His Leu Asn Gln |     |
| 50                                  | 55                      | 60  |
| Met Ser Gln Glu Phe Leu Gln Gln Ser | Leu Lys Glu Gly Glu Ala |     |
| 65                                  | 70                      | 75  |
| Ala Leu His Tyr Phe Glu Glu Leu Pro | Ser Ala Asn Gly Ser Val |     |
| 80                                  | 85                      | 90  |
| Pro Ile Val Trp Gln Ala Thr Pro Arg | Pro Trp Leu Val Ile Thr |     |
| 95                                  | 100                     | 105 |
| Ile Ile Thr Val Asp Arg Gln Pro Gly | Phe His Tyr Val Leu Gln |     |
| 110                                 | 115                     | 120 |
| Val Val Ser Gln Phe His Arg Leu Leu | Gln Gln Cys Gly Pro Gln |     |
| 125                                 | 130                     | 135 |
| Cys Glu Gly His Gln Leu Phe Leu Cys | Asn Val Glu Arg Ser Val |     |
| 140                                 | 145                     | 150 |
| Ser His Phe Asp Ala Lys Leu Leu Ser | Lys Tyr Val Pro Val Ala |     |
| 155                                 | 160                     | 165 |
| Asn Arg Tyr Glu Gly Thr Glu Asp Asp | Tyr Gly Asp Asp Pro Ser |     |
| 170                                 | 175                     | 180 |
| Thr Asn Ser Phe Glu Lys Glu Lys Gln | Asp Tyr Val Tyr Cys Leu |     |
| 185                                 | 190                     | 195 |
| Glu Ser Ser Leu Gln Thr Tyr Asn Pro | Asp Tyr Val Leu Met Val |     |
| 200                                 | 205                     | 210 |
| Glu Asp Asp Ala Val Pro Glu Glu Gln | Ile Phe Pro Val Leu Glu |     |
| 215                                 | 220                     | 225 |
| His Leu Leu Arg Ala Arg Phe Ser Glu | Pro His Leu Arg Asp Ala |     |
| 230                                 | 235                     | 240 |
| Leu Tyr Leu Lys Leu Tyr His Pro Glu | Arg Leu Gln His Tyr Ile |     |
| 245                                 | 250                     | 255 |
| Asn Pro Glu Pro Met Arg Ile Leu Glu | Trp Val Gly Val Gly Met |     |
| 260                                 | 265                     | 270 |
| Leu Leu Gly Pro Leu Leu Thr Trp Ile | Tyr Met Arg Phe Ala Ser |     |
| 275                                 | 280                     | 285 |
| Arg Pro Gly Phe Ser Trp Pro Val Met | Leu Phe Phe Ser Leu Tyr |     |
| 290                                 | 295                     | 300 |
| Ser Met Gly Leu Val Glu Leu Val Gly | Arg His Tyr Phe Leu Glu |     |
| 305                                 | 310                     | 315 |
| Leu Arg Arg Leu Ser Pro Ser Leu Tyr | Ser Val Val Pro Ala Ser |     |
| 320                                 | 325                     | 330 |
| Gln Cys Cys Thr Pro Ala Met Leu Phe | Pro Ala Pro Ala Ala Arg |     |
| 335                                 | 340                     | 345 |
| Arg Thr Leu Thr Tyr Leu Ser Gln Val | Tyr Cys His Lys Gly Phe |     |
| 350                                 | 355                     | 360 |
| Gly Lys Asp Met Ala Leu Tyr Ser Leu | Leu Arg Ala Lys Gly Glu |     |
| 365                                 | 370                     | 375 |
| Arg Ala Tyr Val Val Glu Pro Asn Leu | Val Lys His Ile Gly Leu |     |
| 380                                 | 385                     | 390 |
| Phe Ser Ser Leu Arg Tyr Asn Phe His | Pro Ser Leu Leu         |     |
| 395                                 | 400                     |     |

&lt;210&gt; 118

&lt;211&gt; 131

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2253036

&lt;400&gt; 118

```

Met Glu Arg Cys Phe His Cys Phe Pro Val His Leu Val Phe Asn
 1           5           10           15
Leu Val Gln Ser Phe Ser Pro Ile Ser Gly Val Glu Ser Cys Leu
           20           25           30
Leu Pro Gln Cys Asp Lys Cys Trp Pro Met Val Tyr Arg Ser Cys
           35           40           45
Asp Ala Ser Arg Gly Leu Val Asn Ala Cys Ile Leu Gly Phe Val
           50           55           60
Leu Leu Glu Cys Ser Phe Val Gly Ala Leu Asn Asn Tyr Val Arg
           65           70           75
Ser Leu Ala Thr Leu Leu Glu Arg Thr His Gly Gly Lys Arg Leu
           80           85           90
Lys Leu Cys Glu Glu Ser Gln Ala Ser His Pro Ser Phe Ser Ala
           95          100          105
Glu Pro Arg His Gln Pro Thr Cys Gln Leu Asn Ala Thr Val Arg
          110          115          120
Val Ile Thr Ser Lys Ile Thr Arg Lys Thr Thr
          125          130

```

&lt;210&gt; 119

&lt;211&gt; 556

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2280161

&lt;400&gt; 119

```

Met Ala Ala Ala Ala Trp Leu Gln Val Leu Pro Val Ile Leu Leu
 1           5           10           15
Leu Leu Gly Ala His Pro Ser Pro Leu Ser Phe Phe Ser Ala Gly
           20           25           30
Pro Ala Thr Val Ala Ala Ala Asp Arg Ser Lys Trp His Ile Pro
           35           40           45
Ile Pro Ser Gly Lys Asn Tyr Phe Ser Phe Gly Lys Ile Leu Phe
           50           55           60
Arg Asn Thr Thr Ile Phe Leu Lys Phe Asp Gly Glu Pro Cys Asp
           65           70           75
Leu Ser Leu Asn Ile Thr Trp Tyr Leu Lys Ser Ala Asp Cys Tyr
           80           85           90
Asn Glu Ile Tyr Asn Phe Lys Ala Glu Glu Val Glu Leu Tyr Leu
           95          100          105
Glu Lys Leu Lys Glu Lys Arg Gly Leu Ser Gly Lys Tyr Gln Thr
          110          115          120
Ser Ser Lys Leu Phe Gln Asn Cys Ser Glu Leu Phe Lys Thr Gln
          125          130          135
Thr Phe Ser Gly Asp Phe Met His Arg Leu Pro Leu Leu Gly Glu
          140          145          150

```

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Lys | Gln | Glu | Ala | Lys | Glu | Asn | Gly | Thr | Asn | Leu | Thr | Phe | Ile | Gly |  |
|     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |  |
| Asp | Lys | Thr | Ala | Met | His | Glu | Pro | Leu | Gln | Thr | Trp | Gln | Asp | Ala |  |
|     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |  |
| Pro | Tyr | Ile | Phe | Ile | Val | His | Ile | Gly | Ile | Ser | Ser | Ser | Lys | Glu |  |
|     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |  |
| Ser | Ser | Lys | Glu | Asn | Ser | Leu | Ser | Asn | Leu | Phe | Thr | Met | Thr | Val |  |
|     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |  |
| Glu | Val | Lys | Gly | Pro | Tyr | Glu | Tyr | Leu | Thr | Leu | Glu | Asp | Tyr | Pro |  |
|     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |  |
| Leu | Met | Ile | Phe | Phe | Met | Val | Met | Cys | Ile | Val | Tyr | Val | Leu | Phe |  |
|     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| Gly | Val | Leu | Trp | Leu | Ala | Trp | Ser | Ala | Cys | Tyr | Trp | Arg | Asp | Leu |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |  |
| Leu | Arg | Ile | Gln | Phe | Trp | Ile | Gly | Ala | Val | Ile | Phe | Leu | Gly | Met |  |
|     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |  |
| Leu | Glu | Lys | Ala | Val | Phe | Tyr | Ala | Glu | Phe | Gln | Asn | Ile | Arg | Tyr |  |
|     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |  |
| Lys | Gly | Glu | Ser | Val | Gln | Gly | Ala | Leu | Ile | Leu | Ala | Glu | Leu | Leu |  |
|     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |  |
| Ser | Ala | Val | Lys | Arg | Ser | Leu | Ala | Arg | Thr | Leu | Val | Ile | Ile | Val |  |
|     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |  |
| Ser | Leu | Gly | Tyr | Gly | Ile | Val | Lys | Pro | Arg | Leu | Gly | Val | Thr | Leu |  |
|     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |  |
| His | Lys | Val | Val | Val | Ala | Gly | Ala | Leu | Tyr | Leu | Leu | Phe | Ser | Gly |  |
|     |     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |  |
| Met | Glu | Gly | Val | Leu | Arg | Val | Thr | Gly | Tyr | Phe | Ser | Tyr | Pro | Leu |  |
|     |     |     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |  |
| Thr | Leu | Ile | Val | Asn | Leu | Ala | Leu | Ser | Ala | Val | Asp | Ala | Cys | Val |  |
|     |     |     |     | 365 |     |     |     |     | 370 |     |     |     |     | 375 |  |
| Ile | Leu | Trp | Ile | Phe | Ile | Ser | Leu | Thr | Gln | Thr | Met | Lys | Leu | Leu |  |
|     |     |     |     | 380 |     |     |     |     | 385 |     |     |     |     | 390 |  |
| Lys | Leu | Arg | Arg | Asn | Ile | Val | Lys | Leu | Ser | Leu | Tyr | Arg | His | Phe |  |
|     |     |     |     | 395 |     |     |     |     | 400 |     |     |     |     | 405 |  |
| Thr | Asn | Thr | Leu | Ile | Leu | Ala | Val | Ala | Ala | Ser | Ile | Val | Phe | Ile |  |
|     |     |     |     | 410 |     |     |     |     | 415 |     |     |     |     | 420 |  |
| Ile | Trp | Thr | Thr | Met | Lys | Phe | Arg | Ile | Val | Thr | Cys | Gln | Ser | Asp |  |
|     |     |     |     | 425 |     |     |     |     | 430 |     |     |     |     | 435 |  |
| Trp | Arg | Glu | Leu | Trp | Val | Asp | Asp | Ala | Ile | Trp | Arg | Leu | Leu | Phe |  |
|     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |     | 450 |  |
| Ser | Met | Ile | Leu | Phe | Val | Ile | Met | Val | Leu | Trp | Arg | Pro | Ser | Ala |  |
|     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     | 465 |  |
| Asn | Asn | Gln | Arg | Phe | Ala | Phe | Ser | Pro | Leu | Ser | Glu | Glu | Glu | Glu |  |
|     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |  |
| Glu | Asp | Glu | Gln | Lys | Glu | Pro | Met | Leu | Lys | Glu | Ser | Phe | Glu | Gly |  |
|     |     |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |  |
| Met | Lys | Met | Arg | Ser | Thr | Lys | Gln | Glu | Pro | Asn | Gly | Asn | Ser | Lys |  |
|     |     |     |     | 500 |     |     |     |     | 505 |     |     |     |     | 510 |  |
| Val | Asn | Lys | Ala | Gln | Glu | Asp | Asp | Leu | Lys | Trp | Val | Glu | Glu | Asn |  |
|     |     |     |     | 515 |     |     |     |     | 520 |     |     |     |     | 525 |  |
| Val | Pro | Ser | Ser | Val | Thr | Asp | Val | Ala | Leu | Pro | Ala | Leu | Leu | Asp |  |
|     |     |     |     | 530 |     |     |     |     | 535 |     |     |     |     | 540 |  |
| Ser | Asp | Glu | Glu | Arg | Met | Ile | Thr | His | Phe | Glu | Arg | Ser | Lys | Met |  |
|     |     |     |     | 545 |     |     |     |     | 550 |     |     |     |     | 555 |  |

Glu

<210> 120  
 <211> 514  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2287485

<400> 120  
 Met Ser Trp Pro Arg Arg Leu Leu Leu Arg Tyr Leu Phe Pro Ala  
     1                    5                    10                    15  
 Leu Leu Leu His Gly Leu Gly Glu Gly Ser Ala Leu Leu His Pro  
                     20                    25                    30  
 Asp Ser Arg Ser His Pro Arg Ser Leu Glu Lys Ser Ala Trp Arg  
                     35                    40                    45  
 Ala Phe Lys Glu Ser Gln Cys His His Met Leu Lys His Leu His  
                     50                    55                    60  
 Asn Gly Ala Arg Ile Thr Val Gln Met Pro Pro Thr Ile Glu Gly  
                     65                    70                    75  
 His Trp Val Ser Thr Gly Cys Glu Val Arg Ser Gly Pro Glu Phe  
                     80                    85                    90  
 Ile Thr Arg Ser Tyr Arg Phe Tyr His Asn Asn Thr Phe Lys Ala  
                     95                    100                    105  
 Tyr Gln Phe Tyr Tyr Gly Ser Asn Arg Cys Thr Asn Pro Thr Tyr  
                     110                    115                    120  
 Thr Leu Ile Ile Arg Gly Lys Ile Arg Leu Arg Gln Ala Ser Trp  
                     125                    130                    135  
 Ile Ile Arg Gly Gly Thr Glu Ala Asp Tyr Gln Leu His Asn Val  
                     140                    145                    150  
 Gln Val Ile Cys His Thr Glu Ala Val Ala Glu Lys Leu Gly Gln  
                     155                    160                    165  
 Gln Val Asn Arg Thr Cys Pro Gly Phe Leu Ala Asp Gly Gly Pro  
                     170                    175                    180  
 Trp Val Gln Asp Val Ala Tyr Asp Leu Trp Arg Glu Glu Asn Gly  
                     185                    190                    195  
 Cys Glu Cys Thr Lys Ala Val Asn Phe Ala Met His Glu Leu Gln  
                     200                    205                    210  
 Leu Ile Arg Val Glu Lys Gln Tyr Leu His His Asn Leu Asp His  
                     215                    220                    225  
 Leu Val Glu Glu Leu Phe Leu Gly Asp Ile His Thr Asp Ala Thr  
                     230                    235                    240  
 Gln Arg Met Phe Tyr Arg Pro Ser Ser Tyr Gln Pro Pro Leu Gln  
                     245                    250                    255  
 Asn Ala Lys Asn His Asp His Ala Cys Ile Ala Cys Arg Ile Ile  
                     260                    265                    270  
 Tyr Arg Ser Asp Glu His His Pro Pro Ile Leu Pro Pro Lys Ala  
                     275                    280                    285  
 Asp Leu Thr Ile Gly Leu His Gly Glu Trp Val Ser Gln Arg Cys  
                     290                    295                    300  
 Glu Val Arg Pro Glu Val Leu Phe Leu Thr Arg His Phe Ile Phe  
                     305                    310                    315  
 His Asp Asn Asn Asn Thr Trp Glu Gly His Tyr Tyr His Tyr Ser  
                     320                    325                    330  
 Asp Pro Val Cys Lys His Pro Thr Phe Ser Ile Tyr Ala Arg Gly  
                     335                    340                    345

```

Arg Tyr Ser Arg Gly Val Leu Ser Ser Arg Val Met Gly Gly Thr
      350                      355                      360
Glu Phe Val Phe Lys Val Asn His Met Lys Val Thr Pro Met Asp
      365                      370                      375
Ala Ala Thr Ala Ser Leu Leu Asn Val Phe Asn Gly Asn Glu Cys
      380                      385                      390
Gly Ala Glu Gly Ser Trp Gln Val Gly Ile Gln Gln Asp Val Thr
      395                      400                      405
His Thr Asn Gly Cys Val Ala Leu Gly Ile Lys Leu Pro His Thr
      410                      415                      420
Glu Tyr Glu Ile Phe Lys Met Glu Gln Asp Ala Arg Gly Arg Tyr
      425                      430                      435
Leu Leu Phe Asn Gly Gln Arg Pro Ser Asp Gly Ser Ser Pro Asp
      440                      445                      450
Arg Pro Glu Lys Arg Ala Thr Ser Tyr Gln Met Pro Leu Val Gln
      455                      460                      465
Cys Ala Ser Ser Ser Pro Arg Ala Glu Asp Leu Ala Glu Asp Ser
      470                      475                      480
Gly Ser Ser Leu Tyr Gly Arg Ala Pro Gly Arg His Thr Trp Ser
      485                      490                      495
Leu Leu Leu Ala Ala Leu Ala Cys Leu Val Pro Leu Leu His Trp
      500                      505                      510
Asn Ile Arg Arg

```

&lt;210&gt; 121

&lt;211&gt; 109

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2380344

&lt;400&gt; 121

```

Met Leu Trp Trp Leu Val Leu Leu Leu Leu Pro Thr Leu Lys Ser
  1                      5                      10                      15
Val Phe Cys Ser Leu Val Thr Ser Leu Tyr Leu Pro Asn Thr Glu
      20                      25                      30
Asp Leu Ser Leu Trp Leu Trp Pro Lys Pro Asp Leu His Ser Gly
      35                      40                      45
Thr Arg Thr Glu Val Ser Thr His Thr Val Pro Ser Lys Pro Gly
      50                      55                      60
Thr Ala Ser Pro Cys Trp Pro Leu Ala Gly Ala Val Pro Ser Pro
      65                      70                      75
Thr Val Ser Arg Leu Glu Ala Leu Thr Arg Ala Val Gln Val Ala
      80                      85                      90
Glu Pro Leu Gly Ser Cys Gly Phe Gln Gly Gly Pro Cys Pro Gly
      95                      100                      105
Arg Arg Arg Asp

```

&lt;210&gt; 122

<211> 431  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2383171

<400> 122

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| Met | Ser | Trp | Val | Gln | Ala | Thr | Leu | Leu | Ala | Arg | Gly | Leu | Cys | Arg | 1   | 5   | 10  | 15 |
| Ala | Trp | Gly | Gly | Thr | Cys | Gly | Ala | Ala | Leu | Thr | Gly | Thr | Ser | Ile | 20  | 25  | 30  |    |
| Ser | Gln | Val | Pro | Arg | Arg | Leu | Pro | Arg | Gly | Leu | His | Cys | Ser | Ala | 35  | 40  | 45  |    |
| Ala | Ala | His | Ser | Ser | Glu | Gln | Ser | Leu | Val | Pro | Ser | Pro | Pro | Glu | 50  | 55  | 60  |    |
| Pro | Arg | Gln | Arg | Pro | Thr | Lys | Ala | Leu | Val | Pro | Phe | Glu | Asp | Leu | 65  | 70  | 75  |    |
| Phe | Gly | Gln | Ala | Pro | Gly | Gly | Glu | Arg | Asp | Lys | Ala | Ser | Phe | Leu | 80  | 85  | 90  |    |
| Gln | Thr | Val | Gln | Lys | Phe | Ala | Glu | His | Ser | Val | Arg | Lys | Arg | Gly | 95  | 100 | 105 |    |
| His | Ile | Asp | Phe | Ile | Tyr | Leu | Ala | Leu | Arg | Lys | Met | Arg | Glu | Tyr | 110 | 115 | 120 |    |
| Gly | Val | Glu | Arg | Asp | Leu | Ala | Val | Tyr | Asn | Gln | Leu | Leu | Asn | Ile | 125 | 130 | 135 |    |
| Phe | Pro | Lys | Glu | Val | Phe | Arg | Pro | Arg | Asn | Ile | Ile | Gln | Arg | Ile | 140 | 145 | 150 |    |
| Phe | Val | His | Tyr | Pro | Arg | Gln | Gln | Glu | Cys | Gly | Ile | Ala | Val | Leu | 155 | 160 | 165 |    |
| Glu | Gln | Met | Glu | Asn | His | Gly | Val | Met | Pro | Asn | Lys | Glu | Thr | Glu | 170 | 175 | 180 |    |
| Phe | Leu | Leu | Ile | Gln | Ile | Phe | Gly | Arg | Lys | Ser | Tyr | Pro | Met | Leu | 185 | 190 | 195 |    |
| Lys | Leu | Val | Arg | Leu | Lys | Leu | Trp | Phe | Pro | Arg | Phe | Met | Asn | Val | 200 | 205 | 210 |    |
| Asn | Pro | Phe | Pro | Val | Pro | Arg | Asp | Leu | Pro | Gln | Asp | Pro | Val | Glu | 215 | 220 | 225 |    |
| Leu | Ala | Met | Phe | Gly | Leu | Arg | His | Met | Glu | Pro | Asp | Leu | Ser | Ala | 230 | 235 | 240 |    |
| Arg | Val | Thr | Ile | Tyr | Gln | Val | Pro | Leu | Pro | Lys | Asp | Ser | Thr | Gly | 245 | 250 | 255 |    |
| Ala | Ala | Asp | Pro | Pro | Gln | Pro | His | Ile | Val | Gly | Ile | Gln | Ser | Pro | 260 | 265 | 270 |    |
| Asp | Gln | Gln | Ala | Ala | Leu | Ala | Arg | His | Asn | Pro | Ala | Arg | Pro | Val | 275 | 280 | 285 |    |
| Phe | Val | Glu | Gly | Pro | Phe | Ser | Leu | Trp | Leu | Arg | Asn | Lys | Cys | Val | 290 | 295 | 300 |    |
| Tyr | Tyr | His | Ile | Leu | Arg | Ala | Asp | Leu | Leu | Pro | Pro | Glu | Glu | Arg | 305 | 310 | 315 |    |
| Glu | Val | Glu | Glu | Thr | Pro | Glu | Glu | Trp | Asn | Leu | Tyr | Tyr | Pro | Met | 320 | 325 | 330 |    |
| Gln | Leu | Asp | Leu | Glu | Tyr | Val | Arg | Ser | Gly | Trp | Asp | Asn | Tyr | Glu | 335 | 340 | 345 |    |
| Phe | Asp | Ile | Asn | Glu | Val | Glu | Glu | Gly | Pro | Val | Phe | Ala | Met | Cys | 350 | 355 | 360 |    |

```

Met Ala Gly Ala His Asp Gln Ala Thr Met Ala Lys Trp Ile Gln
      365                      370                      375
Gly Leu Gln Glu Thr Asn Pro Thr Leu Ala Gln Ile Pro Val Val
      380                      385                      390
Phe Arg Leu Ala Gly Ser Thr Arg Glu Leu Gln Thr Ser Ser Ala
      395                      400                      405
Gly Leu Glu Glu Pro Pro Leu Pro Glu Asp His Gln Glu Glu Asp
      410                      415                      420
Asp Asn Leu Gln Arg Gln Gln Gln Gly Gln Ser
      425                      430

```

```

<210> 123
<211> 142
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 2396046

```

```

<400> 123
Met Leu Leu Gly Val Arg Ala Val Pro Leu Cys Ser Ala Trp Gln
  1          5          10          15
Gly Ala Val Gly Leu Val Ser Leu Ala Ile Ser Ile Cys Lys His
      20          25          30
Gly Leu Ser Ser Gln Gln Asn Leu Val Pro Gly Lys Ser Asn Val
      35          40          45
Pro Lys Ala Ser Asp Met Pro Arg Cys Pro Pro Val Phe Gln Ser
      50          55          60
Pro Asn Leu Thr Pro Phe Pro His His Thr Lys His Thr Ser Gln
      65          70          75
Gly Ser His Leu Gly Val Pro Pro Pro Ala Pro Met Pro Trp Cys
      80          85          90
Pro Gln Ala Gln Gly Phe Gly Leu Ser Cys Gln Ser Leu Asp Ala
      95          100         105
Phe Glu Gly Gln Leu Gly Cys Gly Trp Gly Val Gln Ala Ala Gly
      110         115         120
Glu Pro Arg Leu Arg Ile Ile His Thr Leu Leu Phe Gly Ala Phe
      125         130         135
Val Glu Val Ser Arg Ile Pro
      140

```

```

<210> 124
<211> 643
<212> PRT
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<223> Incyte Clone No: 2456587

```

<400> 124  
Met Glu Cys Cys Arg Arg Ala Thr Pro Gly Thr Leu Leu Leu Phe  
1 5 10 15  
Leu Ala Phe Leu Leu Leu Ser Ser Arg Thr Ala Arg Ser Glu Glu  
20 25 30  
Asp Arg Asp Gly Leu Trp Asp Ala Trp Gly Pro Trp Ser Glu Cys  
35 40 45  
Ser Arg Thr Cys Gly Gly Gly Ala Ser Tyr Ser Leu Arg Arg Cys  
50 55 60  
Leu Ser Ser Lys Ser Cys Glu Gly Arg Asn Ile Arg Tyr Arg Thr  
65 70 75  
Cys Ser Asn Val Asp Cys Pro Pro Glu Ala Gly Asp Phe Arg Ala  
80 85 90  
Gln Gln Cys Ser Ala His Asn Asp Val Lys His His Gly Gln Phe  
95 100 105  
Tyr Glu Trp Leu Pro Val Ser Asn Asp Pro Asp Asn Pro Cys Ser  
110 115 120  
Leu Lys Cys Gln Ala Lys Gly Thr Thr Leu Val Val Glu Leu Ala  
125 130 135  
Pro Lys Val Leu Asp Gly Thr Arg Cys Tyr Thr Glu Ser Leu Asp  
140 145 150  
Met Cys Ile Ser Gly Leu Cys Gln Ile Val Gly Cys Asp His Gln  
155 160 165  
Leu Gly Ser Thr Val Lys Glu Asp Asn Cys Gly Val Cys Asn Gly  
170 175 180  
Asp Gly Ser Thr Cys Arg Leu Val Arg Gly Gln Tyr Lys Ser Gln  
185 190 195  
Leu Ser Ala Thr Lys Ser Asp Asp Thr Val Val Ala Ile Pro Tyr  
200 205 210  
Gly Ser Arg His Ile Arg Leu Val Leu Lys Gly Pro Asp His Leu  
215 220 225  
Tyr Leu Glu Thr Lys Thr Leu Gln Gly Thr Lys Gly Glu Asn Ser  
230 235 240  
Leu Ser Ser Thr Gly Thr Phe Leu Val Asp Asn Ser Ser Val Asp  
245 250 255  
Phe Gln Lys Phe Pro Asp Lys Glu Ile Leu Arg Met Ala Gly Pro  
260 265 270  
Leu Thr Ala Asp Phe Ile Val Lys Ile Arg Asn Ser Gly Ser Ala  
275 280 285  
Asp Ser Thr Val Gln Phe Ile Phe Tyr Gln Pro Ile Ile His Arg  
290 295 300  
Trp Arg Glu Thr Asp Phe Phe Pro Cys Ser Ala Thr Cys Gly Gly  
305 310 315  
Gly Tyr Gln Leu Thr Ser Ala Glu Cys Tyr Asp Leu Arg Ser Asn  
320 325 330  
Arg Val Val Ala Asp Gln Tyr Cys His Tyr Tyr Pro Glu Asn Ile  
335 340 345  
Lys Pro Lys Pro Lys Leu Gln Glu Cys Asn Leu Asp Pro Cys Pro  
350 355 360  
Ala Ser Asp Gly Tyr Lys Gln Ile Met Pro Tyr Asp Leu Tyr His  
365 370 375  
Pro Leu Pro Arg Trp Glu Ala Thr Pro Trp Thr Ala Cys Ser Ser  
380 385 390  
Ser Cys Gly Gly Gly Ile Gln Ser Arg Ala Val Ser Cys Val Glu  
395 400 405  
Glu Asp Ile Gln Gly His Val Thr Ser Val Glu Glu Trp Lys Cys  
410 415 420

```

Met Tyr Thr Pro Lys Met Pro Ile Ala Gln Pro Cys Asn Ile Phe
      425                      430                      435
Asp Cys Pro Lys Trp Leu Ala Gln Glu Trp Ser Pro Cys Thr Val
      440                      445                      450
Thr Cys Gly Gln Gly Leu Arg Tyr Arg Val Val Leu Cys Ile Asp
      455                      460                      465
His Arg Gly Met His Thr Gly Gly Cys Ser Pro Lys Thr Lys Pro
      470                      475                      480
His Ile Lys Glu Glu Cys Ile Val Pro Thr Pro Cys Tyr Lys Pro
      485                      490                      495
Lys Glu Lys Leu Pro Val Glu Ala Lys Leu Pro Trp Phe Lys Gln
      500                      505                      510
Ala Gln Glu Leu Glu Glu Gly Ala Ala Val Ser Glu Glu Pro Ser
      515                      520                      525
Phe Ile Pro Glu Ala Trp Ser Ala Cys Thr Val Thr Cys Gly Val
      530                      535                      540
Gly Thr Gln Val Arg Ile Val Arg Cys Gln Val Leu Leu Ser Phe
      545                      550                      555
Ser Gln Ser Val Ala Asp Leu Pro Ile Asp Glu Cys Glu Gly Pro
      560                      565                      570
Lys Pro Ala Ser Gln Arg Ala Cys Tyr Ala Gly Pro Cys Ser Gly
      575                      580                      585
Glu Ile Pro Glu Phe Asn Pro Asp Glu Thr Asp Gly Leu Phe Gly
      590                      595                      600
Gly Leu Gln Asp Phe Asp Glu Leu Tyr Asp Trp Glu Tyr Glu Gly
      605                      610                      615
Phe Thr Lys Cys Ser Glu Ser Cys Gly Gly Gly Val Gln Glu Ala
      620                      625                      630
Val Val Ser Cys Leu Asn Lys Gln Thr Arg Glu Pro Cys
      635                      640

```

&lt;210&gt; 125

&lt;211&gt; 568

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2484813

&lt;400&gt; 125

```

Met Val Leu Leu His Trp Cys Leu Leu Trp Leu Leu Phe Pro Leu
  1                      5                      10                      15
Ser Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe
                      20                      25                      30
Gln Met Gln Ile Arg Asp Lys Ala Phe Phe His Asp Ser Ser Val
                      35                      40                      45
Ile Pro Asp Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr
                      50                      55                      60
Pro Lys Arg Tyr Phe Phe Val Val Glu Glu Asp Asn Thr Pro Leu
                      65                      70                      75
Ser Val Thr Val Thr Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu
                      80                      85                      90
Ser Leu Gln Glu Leu Pro Glu Asp Arg Ser Gly Glu Gly Ser Gly

```



|                 |                     |                         |     |  |     |
|-----------------|---------------------|-------------------------|-----|--|-----|
|                 | 95                  |                         | 100 |  | 105 |
| Asp Leu Glu Pro | Leu Glu Gln Gln Lys | Gln Gln Ile Ile Asn Glu |     |  |     |
|                 | 110                 |                         | 115 |  | 120 |
| Glu Gly Thr Glu | Leu Phe Ser Tyr Lys | Gly Asn Asp Val Glu Tyr |     |  |     |
|                 | 125                 |                         | 130 |  | 135 |
| Phe Ile Ser Ser | Ser Ser Pro Ser Gly | Leu Tyr Gln Leu Asp Leu |     |  |     |
|                 | 140                 |                         | 145 |  | 150 |
| Leu Ser Thr Glu | Lys Asp Thr His Phe | Lys Val Tyr Ala Thr Thr |     |  |     |
|                 | 155                 |                         | 160 |  | 165 |
| Thr Pro Glu Ser | Asp Gln Pro Tyr Pro | Glu Leu Pro Tyr Asp Pro |     |  |     |
|                 | 170                 |                         | 175 |  | 180 |
| Arg Val Asp Val | Thr Ser Leu Gly Arg | Thr Thr Val Thr Leu Ala |     |  |     |
|                 | 185                 |                         | 190 |  | 195 |
| Trp Lys Pro Ser | Pro Thr Ala Ser Leu | Leu Lys Gln Pro Ile Gln |     |  |     |
|                 | 200                 |                         | 205 |  | 210 |
| Tyr Cys Val Val | Ile Asn Lys Glu His | Asn Phe Lys Ser Leu Cys |     |  |     |
|                 | 215                 |                         | 220 |  | 225 |
| Ala Val Glu Ala | Lys Leu Ser Ala Asp | Asp Ala Phe Met Met Ala |     |  |     |
|                 | 230                 |                         | 235 |  | 240 |
| Pro Lys Pro Gly | Leu Asp Phe Ser Pro | Phe Asp Phe Ala His Phe |     |  |     |
|                 | 245                 |                         | 250 |  | 255 |
| Gly Phe Pro Ser | Asp Asn Ser Gly Lys | Glu Arg Ser Phe Gln Ala |     |  |     |
|                 | 260                 |                         | 265 |  | 270 |
| Lys Pro Ser Pro | Lys Leu Gly Arg His | Val Tyr Ser Arg Pro Lys |     |  |     |
|                 | 275                 |                         | 280 |  | 285 |
| Val Asp Ile Gln | Lys Ile Cys Ile Gly | Asn Lys Asn Ile Phe Thr |     |  |     |
|                 | 290                 |                         | 295 |  | 300 |
| Val Ser Asp Leu | Lys Pro Asp Thr Gln | Tyr Tyr Phe Asp Val Phe |     |  |     |
|                 | 305                 |                         | 310 |  | 315 |
| Val Val Asn Ile | Asn Ser Asn Met Ser | Thr Ala Tyr Val Gly Thr |     |  |     |
|                 | 320                 |                         | 325 |  | 330 |
| Phe Ala Arg Thr | Lys Glu Glu Ala Lys | Gln Lys Thr Val Glu Leu |     |  |     |
|                 | 335                 |                         | 340 |  | 345 |
| Lys Asp Gly Lys | Ile Thr Asp Val Phe | Val Lys Arg Lys Gly Ala |     |  |     |
|                 | 350                 |                         | 355 |  | 360 |
| Lys Phe Leu Arg | Phe Ala Pro Val Ser | Ser His Gln Lys Val Thr |     |  |     |
|                 | 365                 |                         | 370 |  | 375 |
| Phe Phe Ile His | Ser Cys Leu Asp Ala | Val Gln Ile Gln Val Arg |     |  |     |
|                 | 380                 |                         | 385 |  | 390 |
| Arg Asp Gly Lys | Leu Leu Leu Ser Gln | Asn Val Glu Gly Ile Gln |     |  |     |
|                 | 395                 |                         | 400 |  | 405 |
| Gln Phe Gln Leu | Arg Gly Lys Pro Lys | Ala Lys Tyr Leu Val Arg |     |  |     |
|                 | 410                 |                         | 415 |  | 420 |
| Leu Lys Gly Asn | Lys Lys Gly Ala Ser | Met Leu Lys Ile Leu Ala |     |  |     |
|                 | 425                 |                         | 430 |  | 435 |
| Thr Thr Arg Pro | Thr Lys Gln Ser Phe | Pro Ser Leu Pro Glu Asp |     |  |     |
|                 | 440                 |                         | 445 |  | 450 |
| Thr Arg Ile Lys | Ala Phe Asp Lys Leu | Arg Thr Cys Ser Ser Ala |     |  |     |
|                 | 455                 |                         | 460 |  | 465 |
| Thr Val Ala Trp | Leu Gly Thr Gln Glu | Arg Asn Lys Phe Cys Ile |     |  |     |
|                 | 470                 |                         | 475 |  | 480 |
| Tyr Lys Lys Glu | Val Asp Asp Asn Tyr | Asn Glu Asp Gln Lys Lys |     |  |     |
|                 | 485                 |                         | 490 |  | 495 |
| Arg Glu Gln Asn | Gln Cys Leu Gly Pro | Asp Ile Arg Lys Lys Ser |     |  |     |
|                 | 500                 |                         | 505 |  | 510 |
| Glu Lys Val Leu | Cys Lys Tyr Phe His | Ser Gln Asn Leu Gln Lys |     |  |     |
|                 | 515                 |                         | 520 |  | 525 |

Ala Val Thr Thr Glu Thr Ile Lys Gly Leu Gln Pro Gly Lys Ser  
                           530                          535                          540  
 Tyr Leu Leu Asp Val Tyr Val Ile Gly His Gly Gly His Ser Val  
                           545                          550                          555  
 Lys Tyr Gln Ser Lys Val Val Lys Thr Arg Lys Phe Cys  
                           560                          565

<210> 126  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2493851

<400> 126  
 Met Trp Leu Val Gly Pro Ser Phe Leu Ser Cys Pro Leu Gly Lys  
   1                          5                          10                          15  
 Val Pro Pro Ala Gly Leu Leu Leu Ala Gly Ser Ser Gly Arg Gly  
                           20                          25                          30  
 Ala Arg Arg Pro Ala Thr Pro Arg His Trp Ser Ser Thr Thr Pro  
                           35                          40                          45  
 Gly Leu Arg Leu Glu Ala Pro Leu Cys Gln Leu Cys Pro Leu Gly  
                           50                          55                          60  
 Gly Thr Arg Gln Asp Cys Gln Pro Leu Ser Trp Gln Val Thr Ser  
                           65                          70                          75  
 Ala Phe Lys Leu Thr Val Pro Ser Pro Phe His Ala Pro Pro Arg  
                           80                          85                          90  
 Ser Trp Ser Cys Leu Leu Leu Gly Ile Phe Pro Gly Gln Ala Leu  
                           95                          100                          105  
 Ala Leu Glu Pro Trp His Leu Phe Leu Gly Ser Met Leu Pro Arg  
                           110                          115                          120  
 Cys Asp Gly Glu Cys  
                           125

<210> 127  
 <211> 196  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2495719

<400> 127  
 Met Ala Ala Leu Lys Ala Leu Val Ser Gly Cys Gly Arg Leu Leu  
   1                          5                          10                          15  
 Arg Gly Leu Leu Ala Gly Pro Ala Ala Thr Ser Trp Ser Arg Leu  
                           20                          25                          30  
 Pro Ala Arg Gly Phe Arg Glu Val Val Glu Thr Gln Glu Gly Lys

|                 |                         |                         |     |  |     |
|-----------------|-------------------------|-------------------------|-----|--|-----|
|                 | 35                      |                         | 40  |  | 45  |
| Thr Thr Ile Ile | Glu Gly Arg Ile Thr     | Ala Thr Pro Lys Glu Ser |     |  |     |
|                 | 50                      |                         | 55  |  | 60  |
| Pro Asn Pro Pro | Asn Pro Ser Gly Gln Cys | Pro Ile Cys Arg Trp     |     |  |     |
|                 | 65                      |                         | 70  |  | 75  |
| Asn Leu Lys His | Lys Tyr Asn Tyr Asp     | Asp Val Leu Leu Leu Ser |     |  |     |
|                 | 80                      |                         | 85  |  | 90  |
| Gln Phe Ile Arg | Pro His Gly Gly Met     | Leu Pro Arg Lys Ile Thr |     |  |     |
|                 | 95                      |                         | 100 |  | 105 |
| Gly Leu Cys Gln | Glu Glu His Arg Lys     | Ile Glu Glu Cys Val Lys |     |  |     |
|                 | 110                     |                         | 115 |  | 120 |
| Met Ala His Arg | Ala Gly Leu Leu Pro     | Asn His Arg Pro Arg Leu |     |  |     |
|                 | 125                     |                         | 130 |  | 135 |
| Pro Glu Gly Val | Val Pro Lys Ser Lys     | Pro Gln Leu Asn Arg Tyr |     |  |     |
|                 | 140                     |                         | 145 |  | 150 |
| Leu Thr Arg Trp | Ala Pro Gly Ser Val     | Lys Pro Ile Tyr Lys Lys |     |  |     |
|                 | 155                     |                         | 160 |  | 165 |
| Gly Pro Arg Trp | Asn Arg Val Arg Met     | Pro Val Gly Ser Pro Leu |     |  |     |
|                 | 170                     |                         | 175 |  | 180 |
| Leu Arg Asp Asn | Val Cys Tyr Ser Arg     | Thr Pro Trp Lys Leu Tyr |     |  |     |
|                 | 185                     |                         | 190 |  | 195 |

His

&lt;210&gt; 128

&lt;211&gt; 214

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2614153

&lt;400&gt; 128

|                     |                     |                         |  |  |     |
|---------------------|---------------------|-------------------------|--|--|-----|
| Met Val Leu Gly Gly | Cys Pro Val Ser Tyr | Leu Leu Leu Cys Gly     |  |  |     |
| 1                   | 5                   | 10                      |  |  | 15  |
| Gln Ala Ala Leu Leu | Leu Gly Asn Leu Leu | Leu Leu His Cys Val     |  |  |     |
|                     | 20                  | 25                      |  |  | 30  |
| Ser Arg Ser His Ser | Gln Asn Ala Thr Ala | Glu Pro Glu Leu Thr     |  |  |     |
|                     | 35                  | 40                      |  |  | 45  |
| Ser Ala Gly Ala Ala | Gln Pro Glu Gly Pro | Gly Gly Ala Ala Ser     |  |  |     |
|                     | 50                  | 55                      |  |  | 60  |
| Trp Glu Tyr Gly Asp | Pro His Ser Pro Val | Ile Leu Cys Ser Tyr     |  |  |     |
|                     | 65                  | 70                      |  |  | 75  |
| Leu Pro Asp Glu Phe | Ile Glu Cys Glu Asp | Pro Val Asp His Val     |  |  |     |
|                     | 80                  | 85                      |  |  | 90  |
| Gly Asn Ala Thr Ala | Ser Gln Glu Leu Gly | Tyr Gly Cys Leu Lys     |  |  |     |
|                     | 95                  | 100                     |  |  | 105 |
| Phe Gly Gly Gln Ala | Tyr Ser Asp Val Glu | His Thr Ser Val Gln     |  |  |     |
|                     | 110                 | 115                     |  |  | 120 |
| Cys His Ala Leu Asp | Gly Ile Glu Cys Ala | Ser Pro Arg Thr Phe     |  |  |     |
|                     | 125                 | 130                     |  |  | 135 |
| Leu Arg Glu Asn Lys | Pro Cys Ile Lys Tyr | Thr Gly His Tyr Phe     |  |  |     |
|                     | 140                 | 145                     |  |  | 150 |
| Ile Thr Thr Leu Leu | Tyr Ser Phe Phe     | Leu Gly Cys Phe Gly Val |  |  |     |

|                 |                     |                     |         |  |     |
|-----------------|---------------------|---------------------|---------|--|-----|
|                 | 155                 |                     | 160     |  | 165 |
| Asp Arg Phe Cys | Leu Gly His Thr Gly | Thr Ala Val Gly Lys | Leu     |  |     |
|                 | 170                 |                     | 175     |  | 180 |
| Leu Thr Leu Gly | Gly Leu Gly Ile Trp | Trp Phe Val Asp     | Leu Ile |  |     |
|                 | 185                 |                     | 190     |  | 195 |
| Leu Leu Ile Thr | Gly Gly Leu Met Pro | Ser Asp Gly Ser Asn | Trp     |  |     |
|                 | 200                 |                     | 205     |  | 210 |
| Cys Thr Val Tyr |                     |                     |         |  |     |

<210> 129  
 <211> 88  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2655184

<400> 129

|   |    |    |
|---|----|----|
| Met Ala Cys Phe Ser Phe Phe Leu Cys Phe Leu Val His Leu Leu |    |    |
| 1   | 5  | 10 |
| Ile Lys Met Asn Pro Val Thr Glu Ser Pro Ser Cys Leu Phe Ser |    | 15 |
|   | 20 | 25 |
| Pro Pro Ser Glu Ser Ala Leu Ala Ser Gln Leu Ala Leu Ser Ala |    | 30 |
|   | 35 | 40 |
| Ser Cys Asp Gln Arg Ala Pro Phe Ser Leu Ala Gly Val Val Ser |    | 45 |
|   | 50 | 55 |
| His Asp Pro Gly Trp Pro Val Val Arg Leu His Arg Pro Leu Val |    | 60 |
|   | 65 | 70 |
| Pro Glu His Ala Val Phe Ser Gln Pro Ser Leu Gln Pro         |    | 75 |
|   | 80 | 85 |

<210> 130  
 <211> 260  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2848362

<400> 130

|   |    |    |
|---|----|----|
| Met Pro Asp Pro Leu Phe Ser Ala Val Gln Gly Lys Asp Glu Ile |    |    |
| 1   | 5  | 10 |
| Leu His Lys Ala Leu Cys Phe Cys Pro Trp Leu Gly Lys Gly Gly |    | 15 |
|   | 20 | 25 |
| Met Glu Pro Leu Arg Leu Leu Ile Leu Leu Phe Val Thr Glu Leu |    | 30 |
|   | 35 | 40 |
| Ser Gly Ala His Asn Thr Thr Val Phe Gln Gly Val Ala Gly Gln |    | 45 |
|   | 50 | 55 |
| Ser Leu Gln Val Ser Cys Pro Tyr Asp Ser Met Lys His Trp Gly |    | 60 |

|   |     |  |     |  |     |
|---|-----|--|-----|--|-----|
|   | 65  |  | 70  |  | 75  |
| Arg Arg Lys Ala Trp Cys Arg Gln Leu Gly Glu Lys Gly Pro Cys |     |  |     |  |     |
|   | 80  |  | 85  |  | 90  |
| Gln Arg Val Val Ser Thr His Asn Leu Trp Leu Leu Ser Phe Leu |     |  |     |  |     |
|   | 95  |  | 100 |  | 105 |
| Arg Arg Trp Asn Gly Ser Thr Ala Ile Thr Asp Asp Thr Leu Gly |     |  |     |  |     |
|   | 110 |  | 115 |  | 120 |
| Gly Thr Leu Thr Ile Thr Leu Arg Asn Leu Gln Pro His Asp Ala |     |  |     |  |     |
|   | 125 |  | 130 |  | 135 |
| Gly Leu Tyr Gln Cys Gln Ser Leu His Gly Ser Glu Ala Asp Thr |     |  |     |  |     |
|   | 140 |  | 145 |  | 150 |
| Leu Arg Lys Val Leu Val Glu Val Leu Ala Asp Pro Leu Asp His |     |  |     |  |     |
|   | 155 |  | 160 |  | 165 |
| Arg Asp Ala Gly Asp Leu Trp Phe Pro Gly Glu Ser Glu Ser Phe |     |  |     |  |     |
|   | 170 |  | 175 |  | 180 |
| Glu Asp Ala His Val Glu His Ser Ile Ser Arg Ser Leu Leu Glu |     |  |     |  |     |
|   | 185 |  | 190 |  | 195 |
| Gly Glu Ile Pro Phe Pro Pro Thr Ser Ile Leu Leu Leu Leu Ala |     |  |     |  |     |
|   | 200 |  | 205 |  | 210 |
| Cys Ile Phe Leu Ile Lys Ile Leu Ala Ala Ser Ala Leu Trp Ala |     |  |     |  |     |
|   | 215 |  | 220 |  | 225 |
| Ala Ala Trp His Gly Gln Lys Pro Gly Thr His Pro Pro Ser Glu |     |  |     |  |     |
|   | 230 |  | 235 |  | 240 |
| Leu Asp Cys Gly His Asp Pro Gly Tyr Gln Leu Gln Thr Leu Pro |     |  |     |  |     |
|   | 245 |  | 250 |  | 255 |
| Gly Leu Arg Asp Thr   |     |  |     |  |     |
|   | 260 |  |     |  |     |

&lt;210&gt; 131

&lt;211&gt; 295

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2849906

&lt;400&gt; 131

|   |     |     |     |
|---|-----|-----|-----|
| Met Gly Leu Pro Val Ser Trp Ala Pro Pro Ala Leu Trp Val Leu |     |     |     |
| 1   | 5   | 10  | 15  |
| Gly Cys Cys Ala Leu Leu Ser Leu Trp Ala Leu Cys Thr Ala     |     |     |     |
|   | 20  | 25  | 30  |
| Cys Arg Arg Pro Glu Asp Ala Val Ala Pro Arg Lys Arg Ala Arg |     |     |     |
|   | 35  | 40  | 45  |
| Arg Gln Arg Ala Arg Leu Gln Gly Ser Ala Thr Ala Ala Glu Ala |     |     |     |
|   | 50  | 55  | 60  |
| Ser Leu Leu Arg Arg Thr His Leu Cys Ser Leu Ser Lys Ser Asp |     |     |     |
|   | 65  | 70  | 75  |
| Thr Arg Leu His Glu Leu His Arg Gly Pro Arg Ser Ser Arg Ala |     |     |     |
|   | 80  | 85  | 90  |
| Leu Arg Pro Ala Ser Met Asp Leu Leu Arg Pro His Trp Leu Glu |     |     |     |
|   | 95  | 100 | 105 |
| Val Ser Arg Asp Ile Thr Gly Pro Gln Ala Ala Pro Ser Ala Phe |     |     |     |
|   | 110 | 115 | 120 |

```

Pro His Gln Glu Leu Pro Arg Ala Leu Pro Ala Ala Ala Ala Thr
      125                      130                      135
Ala Gly Cys Ala Gly Leu Glu Ala Thr Tyr Ser Asn Val Gly Leu
      140                      145                      150
Ala Ala Leu Pro Gly Val Ser Leu Ala Ala Ser Pro Val Val Ala
      155                      160                      165
Glu Tyr Ala Arg Val Gln Lys Arg Lys Gly Thr His Arg Ser Pro
      170                      175                      180
Gln Glu Pro Gln Gln Gly Lys Thr Glu Val Thr Pro Ala Ala Gln
      185                      190                      195
Val Asp Val Leu Tyr Ser Arg Val Cys Lys Pro Lys Arg Arg Asp
      200                      205                      210
Pro Gly Pro Thr Thr Asp Pro Leu Asp Pro Lys Gly Gln Gly Ala
      215                      220                      225
Ile Leu Ala Leu Ala Gly Asp Leu Ala Tyr Gln Thr Leu Pro Leu
      230                      235                      240
Arg Ala Leu Asp Val Asp Ser Gly Pro Leu Glu Asn Val Tyr Glu
      245                      250                      255
Ser Ile Arg Glu Leu Gly Asp Pro Ala Gly Arg Ser Ser Thr Cys
      260                      265                      270
Gly Ala Gly Thr Pro Pro Ala Ser Ser Cys Pro Ser Leu Gly Arg
      275                      280                      285
Gly Trp Arg Pro Leu Pro Ala Ser Leu Pro
      290                      295

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&lt;210&gt; 132

&lt;211&gt; 183

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2899137

&lt;400&gt; 132

```

Met Ala Ala Ser Met Ala Arg Gly Gly Val Ser Ala Arg Val Leu
  1           5           10           15
Leu Gln Ala Ala Arg Gly Thr Trp Trp Asn Arg Pro Gly Gly Thr
      20           25           30
Ser Gly Ser Gly Glu Gly Val Ala Leu Gly Thr Thr Arg Lys Phe
      35           40           45
Gln Ala Thr Gly Ser Arg Pro Ala Gly Glu Glu Asp Ala Gly Gly
      50           55           60
Pro Glu Arg Pro Gly Asp Val Val Asn Val Val Phe Val Asp Arg
      65           70           75
Ser Gly Gln Arg Ile Pro Val Ser Gly Arg Val Gly Asp Asn Val
      80           85           90
Leu His Leu Ala Gln Arg His Gly Val Asp Leu Glu Gly Ala Cys
      95          100          105
Glu Ala Ser Leu Ala Cys Ser Thr Cys His Val Tyr Val Ser Glu
      110          115          120
Asp His Leu Asp Leu Leu Pro Pro Pro Glu Glu Arg Glu Asp Asp
      125          130          135
Met Leu Asp Met Ala Pro Leu Leu Gln Glu Asn Ser Arg Leu Gly

```

|                 |                     |                     |     |  |     |
|-----------------|---------------------|---------------------|-----|--|-----|
|                 | 140                 |                     | 145 |  | 150 |
| Cys Gln Ile Val | Leu Thr Pro Glu Leu | Glu Gly Ala Glu Phe | Thr |  |     |
|                 | 155                 |                     | 160 |  | 165 |
| Leu Pro Lys Ile | Thr Arg Asn Phe Tyr | Val Asp Gly His Val | Pro |  |     |
|                 | 170                 |                     | 175 |  | 180 |
| Lys Pro His     |                     |                     |     |  |     |

<210> 133  
 <211> 113  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2986229

<400> 133  
 Met Trp Arg Lys Pro Asp Val Leu Tyr Ser Val Ile Pro Val Thr  
   1                  5                  10                  15  
 Ser Leu Phe Phe Leu Leu Ala Leu Asn Leu Pro Asp Val Phe Gly  
                   20                  25                  30  
 Leu Val Val Leu Pro Leu Glu Leu Lys Leu Arg Ile Phe Arg Leu  
                   35                  40                  45  
 Leu Asp Val Arg Ser Val Leu Ser Leu Ser Ala Val Cys Arg Asp  
                   50                  55                  60  
 Leu Phe Thr Ala Ser Asn Asp Pro Leu Leu Trp Arg Phe Leu Tyr  
                   65                  70                  75  
 Leu Arg Asp Phe Arg Gly Asp Phe Arg Asn Asp Ile Phe Thr Arg  
                   80                  85                  90  
 Lys Gly Ser Tyr Cys Leu Asp Tyr Ser Ala His Gln Lys Phe Leu  
                   95                  100                 105  
 Val Val Gly Phe Phe Cys Cys Lys  
                  110

<210> 134  
 <211> 160  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 3222081

<400> 134  
 Met Gln Arg Val Ser Gly Leu Leu Ser Trp Thr Leu Ser Arg Val  
   1                  5                  10                  15  
 Leu Trp Leu Ser Gly Leu Ser Glu Pro Gly Ala Ala Arg Gln Pro  
                   20                  25                  30  
 Arg Ile Met Glu Glu Lys Ala Leu Glu Val Tyr Asp Leu Ile Arg  
                   35                  40                  45  
 Thr Ile Arg Asp Pro Glu Lys Pro Asn Thr Leu Glu Glu Leu Glu

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     | 50  |     | 55  |     | 60  |     |     |     |     |     |     |     |     |     |
| Val | Val | Ser | Glu | Ser | Cys | Val | Glu | Val | Gln | Glu | Ile | Asn | Glu | Glu |
|     | 65  |     | 70  |     | 75  |     |     |     |     |     |     |     |     |     |
| Glu | Tyr | Leu | Val | Ile | Ile | Arg | Phe | Thr | Pro | Thr | Val | Pro | His | Cys |
|     | 80  |     | 85  |     | 90  |     |     |     |     |     |     |     |     |     |
| Ser | Leu | Ala | Thr | Leu | Ile | Gly | Leu | Cys | Leu | Arg | Val | Lys | Leu | Gln |
|     | 95  |     | 100 |     | 105 |     |     |     |     |     |     |     |     |     |
| Arg | Cys | Leu | Pro | Phe | Lys | His | Lys | Leu | Glu | Ile | Tyr | Ile | Ser | Glu |
|     | 110 |     | 115 |     | 120 |     |     |     |     |     |     |     |     |     |
| Gly | Thr | His | Ser | Thr | Glu | Glu | Asp | Ile | Asn | Lys | Gln | Ile | Asn | Asp |
|     | 125 |     | 130 |     | 135 |     |     |     |     |     |     |     |     |     |
| Lys | Glu | Arg | Val | Ala | Ala | Ala | Met | Glu | Asn | Pro | Asn | Leu | Arg | Glu |
|     | 140 |     | 145 |     | 150 |     |     |     |     |     |     |     |     |     |
| Ile | Val | Glu | Gln | Cys | Val | Leu | Glu | Pro | Asp |     |     |     |     |     |
|     | 155 |     | 160 |     |     |     |     |     |     |     |     |     |     |     |

&lt;210&gt; 135

&lt;211&gt; 865

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 443531

&lt;400&gt; 135

```

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caaaagaaaa atacaaaaaa aaaaa

```

865

&lt;210&gt; 136

&lt;211&gt; 706

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt;

&lt;222&gt; 11, 12

&lt;223&gt; a or g or c or t, unknown, or other

&lt;220&gt;



&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 632860

&lt;400&gt; 136

```

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ttgctggctc agcctgctct ttgtccttc atgggacccc agtggatcct gcagttctgc 180
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atagatgggg ttaccaggat tcaggctaca tggcctgagg caaggtcaca acatgagtga 480
cagaatgtgt cctggaagcc aggcacctc tggggtgtat ttggggcgct caacaaggct 540
tgatcgagct ttgggggtag atctagctat tccatgggga ttcttttcag aattgctgtt 600
ttcggttaact aattccatga ccagggtccat ggcattggat gacattgcgc tacactgttg 660
ctcaccgggg tcaccgctcc tcacagggtg gatggcaagc atgttg 706

```

&lt;210&gt; 137

&lt;211&gt; 801

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 670010

&lt;400&gt; 137

```

acttctacat gggcctcctg ctgctgggtgc tcttctcag cctcctgccg gtggcctaca 60
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cccgggagca cctcccctcc cgaggcagtc tgctcagagg gcctcggccc agaattccag 180
ttctggtttc atgccagcct gtaaaaggcc atggaacttt ggggtgaatca ccgatgccat 240
ttaagagggt tttctgccag gatggaaatg ttaggtcggt ctgtgtctgc gctgttcatt 300
tcagtagcca ccagccacct gtggccgttg agtgcttgaa atgaggaact gagaaaatta 360
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ggggtacatg tgatatttgg atacatgtat acaatatata atgatcaaat cagggttaact 480
gggatatacca tcacatcaaa catttatatt ttattctttt tagacagagt ctactctgt 540
caccaggtc ggagtgcagt ggtgccatct cagcttactg caacctctgc ctgccagggt 600
caagcgattc tcatgcctcc acctccaag tagctgggac tacaggcatg caccacaatg 660
cccaactaat ttttgatttt ttagtagaga cggggttttg ccatgttgcc caggctggcc 720
ttgaactcct ggcctcaaac aatccacttg cctcggcctc ccaaagtgtt atgattacag 780
gcgtgagcca ccgtgcctgg g 801

```

&lt;210&gt; 138

&lt;211&gt; 664

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt;

&lt;222&gt; 505, 518, 527, 540, 565, 566

&lt;223&gt; a or g or c or t, unknown, or other

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 726498

&lt;400&gt; 138

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gcagagccat gatgagtctt acggaaataa ggttaaaaca tatgcttgaa atttggcatg 180
gcagacaagc cagagcttgt gaaaatctaa gaaaccaaac acgtgtagcc accaaagtgg 240
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ttgtgcagtc aagcatcttg tgggtgggtct ggagctgttg ccagcatcag gaagacaagc 360
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ggaaatggag taccagata cccanngtga tatactttta tgccctcagt ttcttatctt 600
tcagtgggga taatatcctc ggatacaaaa gagtgtacat atataccctg tatttggtaa 660
acta
664

```

&lt;210&gt; 139

&lt;211&gt; 1241

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 795064

&lt;400&gt; 139

```

ccaggcaata tctcaggata tggaagtttc tgggtttatt taccctcag tgccagagt 60
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gctgaatcgg ggttaacatc ccttcaggc acagcgagt ggttctgctt ttgacctgta 180
agccaaagaa aagccacatc taaaaagcta ctactaaaag ccagaaagaa aagtggattt 240
gaactcagtg tcaacagact ttctgagtgt tttaggggtca cagctagtgt aagaggcatg 300
aagaatagac atgcaaaaagg gaacgggtgc accagagacc cctgttttgg ctgacagacc 360
atatgtcca ccagctgggg aatctgacaa gaggacatag gtggcactct ttttttaaag 420
ctattttatt tatctatttt taaataaaat tgccatcct cattcagctc ttagaacaaa 480
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gatagggcaa ccctgagctt aaacaatgac atcttcaagg gtagaactaa tctgaaaccc 600
ccttcagcc tctggaagac actggcctgc atcagttaga gtcagagcaa gtgtcacttc 660
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taaaaaaagc tcaaaacagt gttaaaaggaa tgaacagtag aattttaata ggctgtccaa 780
agaagccagg tctgctgtgg gcaagtatag cctaacccta gtcttgtaaa ataagccaga 840
aagggttact gagccacctt aagctagtac ctatatagta ggcaaaaagt acagaaatag 900
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tatcacttga gaacctcctc agcaaagatg ccagaaaaca ttcaatcaag ttggcaaatg 1020
acacaggggag ctggccctct gaccatcttc ctggcaaac tggactggaa gggccatttg 1080
cagcactgtc ctggagctaa tacactgttt cactgcctct gccatataat gatgccagca 1140
ctagccagct ggtgggtatt tggaggaatc ctgcatgagg attgcccaat aaggggcagg 1200
tacacatacc tggcaaatg atgatgatgt gaattgtttc c
1241

```

&lt;210&gt; 140

&lt;211&gt; 750

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt;

&lt;222&gt; 570, 641

&lt;223&gt; a or g or c or t, unknown, or other

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 924925

&lt;400&gt; 140

```

tggagtgggg agaagagcat acgccaggag cctcctgcct caaagtgtct ccctaagtct 60
tcttcctcct gtgctgacct cagggtgggtc tgacccttcc ctcggtgtgg gggatgtggc 120
cctctcaggt gcccctactt gctttctgct tccttctggt gaagtccacc tccaacatta 180
acctgccac cccacccccg tcatccctgg agaattccag ctttgtcgta tctcagagag 240
ggaatctaata tgtttttggg gggcaaaaga aagcaacgtt taggtatcac ttctacttgg 300
accgcatgcc tttttatagc caaatctctg tgtatttcgt aaatggattt cgcgttaatg 360
gatatttatg taataactag acttctcaga ttattgtgag aagggtcagg ttggaagggg 420
tgtaggaaga cgggtgaggg gtagtttttt tctgtcctag tttttttttt ttttattgtc 480
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tgtggaagca tcagatgcca gactgactt cagaccagca ntctgggcta gaggaagatg 660
ggacctttca ggatggaaat accttggaact ttcttttggg ccctcggaac cttgggcttt 720
ctctaccgac ttgccagat ttcatttcac

```

750

&lt;210&gt; 141

&lt;211&gt; 1235

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 962390

&lt;400&gt; 141

```

ccctcaggca gcccctccac aggaccctc tcctgcctgg acagctctgc tggctctccc 60
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atgggggtcac tcaacaaaa cacctctcag cctccatggg tggctctgtg gaaatccctt 240
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gatcagggag gcagcagttg cagtcctatc aggggaccaa actcaccatc acccaggctg 540
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cagaaagcaa agggcactca gaatcatggc acctaatgtc ggacactgcc atcagggttg 660
cattggctgt cgctgtgctc aaaactgtca ttttgggact gctgtgcctc ctctcctgt 720
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tccacatttt ccaatctgta tgggtggctgt cttctatggc agaaggtttt ggggaataaa 1200
tagcgtgaaa tgctgctgac acttaaaaaa aaaaa

```

1235

&lt;210&gt; 142

&lt;211&gt; 1834

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1259405

&lt;400&gt; 142

```

gacggaagtg cgggcggagg atccccagcc ggggtcccaag cctgtgcctg tgcctgagcc 60
tgagcctgag cctgagcccc agccgggagc cggtcgcggg ggctccgggc tgtgggaccg 120
ctgggccccc agcgatggcg accctgtggg gaggccttct tcggcttggc tcttgtctca 180
gcctgtcgtg cctggcgctt tccgtgctgc tgcctggcgca gctgtcagac gccgccaaga 240
atctcgagga tgtcagatgt aaatgtatct gccctcccta taaagaaaat tctgggcata 300
tttataataa gaacatatct cagaaagatt gtgattgcct tcatgttgtg gagcccatgc 360
ctgtgcgggg gcctgatgta gaagcatact gtctacgtcg tgaatgcaaa tatgaagaaa 420
gaagctctgt cacaatcaag gttaccatta taatttatct ctccattttg ggcttcttac 480
ttctgtacat ggtatatctt actctggttg agcccatact gaagaggcgc ctctttggac 540
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ctgtataatg agagagaaga tctgatgaga taac 1834

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&lt;210&gt; 143

&lt;211&gt; 1722

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1297384

&lt;400&gt; 143

```

tacgagaccc ggccgcaccc cgagtcacac agggcccccg ggccaaggcg ttcgtctctc 60
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```

&lt;210&gt; 144

&lt;211&gt; 1741

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1299627

&lt;400&gt; 144

```

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cacaattaag atactgacat caaattgttg ccttttacca aaatgcaaat tttatgaagt 1680
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a 1741

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<210> 145
<211> 997
<212> DNA
<213> Homo sapiens

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<220>
<221>
<222> 973
<223> a or g or c or t, unknown, or other

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<220>
<221> misc_feature
<223> Incyte Clone No: 1306026

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<400> 145
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tgctacggac gacgcctatg aagcccttag tccttctagt tgcgcttttg ctatggcctt 180
cgtctgtgcc ggcttatccg agcataactg tgacacctga tgaagagcaa aacttgaatc 240
attatataca agtttttagag aacctagtac gaagtgttcc ctctggggag ccaggctcgtg 300
agaaaaaatc taactctcca aaacatgttt attctatagc atcaaaggga tcaaaattta 360
aggagctagt tacacatgga gacgcttcaa ctgagaatga tgttttaacc aatcctatca 420
gtgaagaaac tacaactttc cctacaggag gcttcacacc ggaaatagga aagaaaaaac 480
acacggaaaag taccctattc tggtcgatca aaccaaacaa tgtttccatt gttttgcatg 540
cagaggaacc ttatatgaa aatgaagagc cagagccaga gccggagcca gctgcaaac 600
aaactgaggc accaagaatg ttgccagttg ttactgaatc atctacaagt ccatatgtta 660
cctcatacaa gtcacctgtc accactttag ataagagcac tggcattgag atctctacag 720
aatcagaaga tgttcctcag ctctcagggt aaactgcat agaaaaaccc gagagttgga 780
agcaccagag agtgggatat gatgcatttg aaaaaaattt agtattaatc acaatgcaca 840
ggcacttcta gtgacacagc acccagctat agagagatat gaaggggtac gagctcgaat 900
tcgaatcatg tcatagctgt ttctgtgtg aattggtatc gctcacaatg cacacacata 960
cgagcggaag ctnaattggt aagcgggggt gccatga 997

```

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<210> 146
<211> 981
<212> DNA
<213> Homo sapiens

```

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<220>
<221> misc_feature
<223> Incyte Clone No: 1316219

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```

<400> 146
gttttaaat tacttaataa atataaaata ttgtatgttc ttaacttgaa gctcatattt 60
tcaagtaatt ccttgtctgg aattttctgt tgatctcatg ggtactaaga aacgaaatat 120
tctgttcatt ttcattttta aagaatatcg ataactgat gacccagaa ggagttggcc 180
ttaccactgc cttacgtgtt ctctgtaatg ttgcatgccc accacctcct gttgaagggtc 240
aacagaaaaga tctgaaatgg aatcttgccg ttattcagct tttttctgct gaaggaatgg 300
acacgtttat tcgagttctg caaaaattga acagtattct gactcagcct tggaggtctc 360

```

```

atgtcaacat ggggactacc cttcacagag ttactactat ttcaatggct cgctgcacac 420
tcactcttct taaaactatg ttaacggaac tcctgagagg tggatccctt gagtttaagg 480
acatgcgtgt tccttcagcg cttgttactt tacatatgct cctgtgctct atccccctct 540
caggtcgttt ggatagtgat gaacagaaaa ttcagaatga tatcattgat attttactga 600
cttttacaca aggagttaat gaaaaactca caatctcaga agagactctg gccaataata 660
cttggctctt aatgttaaaa gaagtctctt cttcaatctt gaagggttct gaaggatttt 720
tttctggact catactcctt tcagagctgc tgcctcttcc attgcccctg caaacaactc 780
aggatctact tccatataac atgcatctta taaatgactg cagtaacact ttttaaaaag 840
ccagtgtatt tgttaaaaaa caaaaaccct catctccctt cctcccaaaa agacataaaa 900
taaccggatg aggggggatg aaaactgaaa caagttggctc attgaggaaa tatgggggta 960
aaaattttta ataaattttt g
981

```

&lt;210&gt; 147

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1329031

&lt;400&gt; 147

```

ctgcaggccc acctgtctgc aaccagctg aggcctatgcc ctccccaggg accgtctgca 60
gcctcctgct cctcggcatg ctctggctgg acttggccat ggcaggctcc agcttcctga 120
gccctgaaca ccagagagtc cagcagagaa aggagtcgaa gaagccacca gccaaactgc 180
agccccgagc tctagcaggc tggctccgcc cggaagatgg aggtcaagca gaaggggagc 240
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aggccaaaga ggcccagcc gacaagtgat cgcccacaag ccttactcac ctctctctaa 420
gtttagaagc gctcatctgg cttttcgctt gcttctgcag caactcccac gactgttgta 480
caagctcagg aggcgaataa atgttccaac ctggtaaaaa aaaaaa 526

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&lt;210&gt; 148

&lt;211&gt; 2090

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1483050

&lt;400&gt; 148

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gaggcgcggg gagagtaggg tgctgtggtc tgagctagag ggtgaagctg gcggagcagg 60
aggatgggcg tatgcaggtg atagactaga gaacaagacc tctgtctccg tagcatcctg 120
gagcagtcctg aatgccagaa tggataaccg ttttgctaca gcatttgtaa ttgcttgtgt 180
gcttagcctc atttccacca tctacatggc agcctccatt ggcacagact tctggtatga 240
atatcgaagt ccagttcaag aaaattccag tgatttgaat aaaagcatct gggatgaatt 300
cattagtgat gaggcagatg aaaagactta taatgatgca ctttttcgat acaatggcac 360
agtgggattg tggagacggg gtatcaccat acccaaaaac atgcattggg atagcccacc 420
agaaaggaca gagtcatttg atgtggtcac aaaatgtgtg agtttcacac taactgagca 480
gttcatggag aaatttgttg atccccgaaa ccacaatagc gggattgatc tccttaggac 540
ctatcttttg cgttgccagt tccttttacc ttttgtgagt ttaggtttga tgtgctttgg 600
ggctttgatc ggactttgtg cttgcatttg ccgaagctta tatcccacca ttgccacggg 660
cattctccat ctcttgcag gtctgtgtac actgggctca gtaagttgtt atgttgcctg 720
aattgaacta ctccaccaga aactagagct ccctgacaat gtatccggtg aatttggatg 780

```

```

gtccttctgc ctggcttgtg tctctgtccc cttacagtcc atggcttctg ctctcttcat 840
ctgggctgct cacaccaacc ggaaagagta caccttaatg aaggcatatc gtgtggcatg 900
agcaagaaac tgcctgcttt acaattgcca tttttatttt tttaaaataa tactgatatt 960
tccccacct ctcaattggt ttttaatttt atttgtggat ataccatttt attatgaaaa 1020
tctattttat ttatacacat tcaccactaa atacacactt aataccacta aaattttatg 1080
ggtttacttt aagcgatgcc atctttcaaa taaactaatc taggtctaga cagaaagaaa 1140
tggatagaga cttgacacaa atttatgaaa gaaaattggg agtaggaatg tgaccgaaaa 1200
caagtgtgct taatgtctgt tagacttttc agtaaaacta aagtaactgt atctgttcaa 1260
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ctataaaatt gggaaattat ctaagatcat tttccctaag cattgacaca tagcttcatc 1440
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tacagtgttt acttgaaatt ttaactttgt aactgcaaga attccagttc agccgggcga 1560
ggattagtat tatttttaac tctccgtaag attttcagta ccaccaaatt gttttggatt 1620
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agaacgtttc accataatga cctccagag ctgggaaacc taccacaaga tctaaagttc 1800
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actgtagcaa ttgacagatt aaaaaaatgt aacttcataa tttcttacca taacctcaat 2040
gtccttttta aaaaataaaa ttaaaaatga aaagagactc aaaaaaaaaa 2090

```

&lt;210&gt; 149

&lt;211&gt; 2403

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1514160

&lt;400&gt; 149

```

gggagagagc agcagagacc tcatcagcag accaaggaag tgggtgggtgc tccccctccc 60
taagctccag ggtccctgaa tcttctgaaa tctcaaatga gtggaggcct cctgggggtg 120
cctgtcctgc aggggcccgt gaatgggggc aagcagctgg gtgggcagaa tgcagagtag 180
actcggggga ggatcctttc actttccgct tccccctctg atgcatggag gatgggtgtg 240
gcttttcagc aggcccgga aggtacgcag gtgacgcctt agcagccccg cagctgggtg 300
tctgccccgc ggtactggcg ccatcagggc ctcccttgcc cgcctgagag cagcagcagt 360
ctctgtcatc ccgtcgcccc ttacccccca cccaggcca ctgggcccct cccacaccac 420
ctggggagct gagaagagga ggctggagta agggaggact tgatcatcca agaaatactt 480
tttattgctg ggagtcttct gaacctcacc aaactgaggc cagagctgag ctcttggggg 540
agttaattca gaggggagag gccagcacct cctcctcca tgcctcgtg tgtgccttaa 600
actccatctc atgtccctcc ccatccctgt gctttccctc cctccttgcc ccatcctggg 660
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tttttttaaa ccaccatgtc actttgagtc cttcatgggt ttttgaacag catttatcaa 1260
gaagaaaatg tgggcttttt cccctctccc gtgttttgtt tgtcctgtag atagagggag 1320
gaaagccgtg cagtggcagg cgggaccccc tctggtggcg ggacccccctc ttgcggtggt 1380

```



```

cttgccggggc cagccggggac ctgtcacttt attatttaag gagtgtgtgt gtagagtgcg 1440
tggcttatta acagtattgt gtgtggggtg gggttttagt ttgttccttc tttttgaagt 1500
cccttcattt caatccttga ctctctctcc ccttcccttg cccagctctg ttgaatgctg 1560
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tccctgtatt tgtgagactc gcaggagtc ccatctgtag cacaggcaat gccagtgcc 1680
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agtcctcacc tgcaggtgtc ggggtggggg ggggcaagga ggggcaggca cacaccatgt 2220
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tttcaaacat gtaactttta tatgaaaaaa aataaacaca gatgaaagct gaaaaaaaaa 2400
aaa 2403

```

&lt;210&gt; 150

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1603403

&lt;400&gt; 150

```

ggccaccggg acttcagtgt ctctccatc ccaggagcgc agtggccact atgggggtctg 60
ggctgcccc tgcctcctc ttgacctcc ttggcagctc acatggaaca gggccgggta 120
tgactttgca actgaagctg aaggagtctt ttctgacaaa ttcctcctat gaggccagct 180
tcttgggaatt gcttgaaaag ctctgcctcc tctccatct ccttcaggg accagcgtca 240
ccctccacca tgcaagatct caacaccatg ttgtctgcaa cacatgacag ccattgaagc 300
ctgtgtcctt cttggcccgg gcttttgggc cggggatgca ggaggcaggc cccgaccctg 360
tctttcagca ggccccacc ctcttgatg gcaataaata aaattcgta tgctgaattc 420
aaaaaaaaa a 431

```

&lt;210&gt; 151

&lt;211&gt; 2109

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1652303

&lt;400&gt; 151

```

tttgtagcca agtgggagct attttctttt ttgtgcatat agatatttct taaatgaagc 60
tgctttcttg tcttttattt ctaaaagccc cttataccc cactttgtgc agcaaagatc 120
cccgtgcagg tcacagcctg atttgtggc aggctggaca aattcctgag gcacaacttg 180
gcttcagttc agatttcaag ctgtgttggt gttgggacca gcagaaggca aacgtccagc 240
caacacacag gactgtaaga ggactctgag ctacgtgccc tgtgaagacc cccaggcttt 300
gtcataggag gtcgttcagc ttcccaaag tcagaggtga tttgatttgg ggaagactga 360
atattcacac ctaagtctg agcatatcct gagttttact tccttatggc ttgccctcca 420

```

```

agttctctct ctcatacaca cacacaccct tgctccagaa tcaccagaca cctccatggc 480
tccagctatg ggaacagctg cattggggct gcctttctgt ttggcttagg aactttctgtg 540
cttcttgggg cccactcgc gaggcagctc ggaggtgttg actccgattg ggctgcaggc 600
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ctgctggcac aggaaggaga ggcgatcccg gctgaggctt aggaaattgc tggagccggc 780
tccaagcaga taattcactg gggagggttt cagagtcaaa catcattctg cctgtgttg 840
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taatggataa acagaaacac ttagaggtga gaaggctctg cttcaagatc caaggtaaga 1260
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gccagcatct cactatttat tgacagggtg ggctgtgtgt gtgcgcatgt gtgtatacat 1560
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tttatgttgt atcaagcctg aatagaaact gatagcatta aaatactccg ttctctctc 1860
tcttctcgct tcttttttt ttttttttaa atttaggata acacattttt gtttctaaag 1920
tgatttgtga tttgtgctgt ataaactgta taaaagggtt tgtttttaaa ggtggatttt 1980
cattctctcg gggacagtg tgcgaagac atctacattg taagagaaca cagtggaaga 2040
tctgtcctcg atttcaaaaa attattttct ctgtatgatt aaaagtttat tccatttaaa 2100
aaaaaaaaa 2109

```

<210> 152

<211> 1114

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1693358

<400> 152

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aacgcggcgc cgggcccggc cgggccctgg agatggtccc cggcgccgcg ggctggtgtt 120
gtctcgtgct ctggctcccc gcgtgcgctc cggcccacgg cttccgtatc catgattatt 180
tgtactttca agtgcctgag cctggggaca ttcgatacat cttcacagcc acacctgcca 240
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cccccaaggg tgtctcatgc tacaagaaga ggcaagagac agggccccag gcttctggct 900
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```

```
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caataaagct tctcatcagg gttaaaaaaa aaaa 1114
```

&lt;210&gt; 153

&lt;211&gt; 2192

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1707711

&lt;400&gt; 153

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aggttccttg gtgtggctca tgaaatcaca gagctcagag ataccatctt gagaaatcct 180
ccttggtatc atgaaactgg agcagaggaa ttgcaattta gcaggaggtc ctctactggg 240
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aattcctgtc ctatttgaga tgaactatat cctgtacctc tgtgctctgt gtctgcatga 540
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cagcattggg gaatatcag tttaggggaa cagttctagg gagtgagaca tttttgggag 720
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gaataaagcc ttgataccaa aattgggaaa gaacatgtgt ccatttggac caaacgttgt 1260
tggtttttta aaaattttat tttgtttttt tgtttttgtt tttgtttttt ttcatcttaa 1320
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cagatacagt ctccctggcc tataatgaaa ccactaggac tttatacagt tttccttaat 1440
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actaggatct gcatttagaa caagaatcat tatttgcct gaccttttca gtcctacaga 1620
gacgcactct tgggtctttt gtacttgcca tagatgtaac ctaaaaagtt ttggcatatt 1680
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&lt;210&gt; 154

&lt;211&gt; 913

&lt;212&gt; DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1738735

<400> 154

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cccatgcccc gggacttcct ccaccctcac caggacattc ttcccatctc ttgtctcctg 180
tgtgcaagtc cctttctcct ggattccatg tcttgaatgt ttcttaattt acttcctcat 240
tttggcagag gatgtcctcc agttgttttc tgggaatgct aatatgcaag tgaaccagtg 300
acctgcagtt ctgcccacac aggggttaata accaatcaga ttctctcttt tcaagatggg 360
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cccagtggtc atacctggtc tgggaagattc cccatcatct cgaataaaagc tgttggttgc 540
tttaactcca tggagagacc gaatggagtg agcccagcag ggcatgctgg gcaagagagg 600
tcccccgagt cccaaataag aatttcaact agtataaaac gaggcagcga acccacacgt 660
ggaagtctga taccgcttgc agaagggaat tgaatagatg tctccctatt ggtaaggatg 720
tggttttatt gacttgaaat aacaaagccc gcaagcaaca actgatcatc cgcgggatgc 780
tgccacaagg aataattgag cactcattca gacacagggg aaaccactgc ctctttcagt 840
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<210> 155

<211> 480

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1749147

<400> 155

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ttgatggaaa atgcagaggc ccttcctctc tgtgccgtgc ttgtcctctt tacctgcccc 180
gggtggttgg ggggtgttgg gtttcctccc tggagaagat gggggagggt gtcccactcc 240
cagctctggc agaatcaagc tgttgcaagc gtgccttctt catccttctt tacgatcaat 300
cacagtctcc agaagatcag ctcaattgct gtgcagggtta aaactacaga accacatccc 360
aaaggtagct ggtaagaatg ttgaaagat cttccatttc taggaacccc agtcctgctt 420
ctccgcaatg gcacatgctt ccactccatc catactgcag tcgtcaaata aacagatatg 480
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<210> 156

<211> 545

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1817722

<400> 156

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ctgttacaag ctgcttcagc tttagctaata tacattcatt tctccagtta ctccaaagat 120
```

```

ggaatagggg taccatztat gggaagtttg gcagaatttt ttgacatcgc ttcccaaatt 180
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tctcaaagca gacctctcca gtgggattct acacctgcat cactggcat tgcagtattc 300
attgtcatga cacagagtgt tttgctactt tgggaacagt ttgaagatat cagtcatcat 360
agctaccatt cacaccacaa cttagcaggg atcctcctaa ttgttctaag aatttgctta 420
gcattgtcat taggctgtgg actctatcag atcatcacag tggagagaag tacactcaaa 480
agggagttct acatcacatt tgccaaagta tgggtttgga aagaaaatgg tttattctga 540
ttatc
545

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<210> 157

<211> 1746

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1831290

<400> 157

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ctgtggcccc gagcagcgt gctgggtgctg ttgggggtgg cagccagtct gtgtgtgcgc 180
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cccttgccgg acatggcacc cacaaggaag gacaagctgt tgcaattcta cccagcctg 360
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gaagcctaca tagaccccat tgccatggag tattacaact gggggcgggt ctccaagccc 480
ccagaagatg atgatgcaa ttcctacgag aatgtgtctca tttgcaagca gaaaaccaca 540
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1746

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<210> 158

<211> 2011

<212> DNA

<213> Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1831477

&lt;400&gt; 158

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cggcgacatg ggcgccccca cggccccgga ggccggcagc tggcgctggg gatccctgct 180
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cagggtccat ggtgccatgg agctgcaggt gcagacaggc aaagatgcac catccaactg 660
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actacatggg gaaacagggt caaaaaaaaa a 2011
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&lt;210&gt; 159

&lt;211&gt; 480

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt;

&lt;222&gt; 440

&lt;223&gt; a or g or c or t, unknown, or other

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1841607

&lt;400&gt; 159

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ttcctccctt cagtctggct gggagcttag ctctttgggg tcattgctgt gtcaggctgg 120
gttggttcctt ttggtctggt tctgccatgg ccagcgcct tccctctcag aatacataca 180
atccccccct ctgctgggcg tggtgactca tgtctataat ccagctctt tgggaggcca 240
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ctacttggga ggctgaggca ggaggatcct tgagcccagg aggcagaagc tgcagtgagc 420
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<210> 160

<211> 542

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1852391

<400> 160

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cccacgtggg aaggccagcg ggaaaccagg cctgctgaag tctccagcgc tggagcctc 180
acgggggtta ggaaggagcc ttgggagcag ctccctcagag cacagtgtga cctcaattgt 240
ggattttaga tgtttctgct tctcaatgtt ctctcttttt tctgctgtgc ttgctgtcct 300
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cgtgattggt tatgtgtatg ttgcaaaact aattcctttt tctacatctg attctttcta 420
cttttgttta gagttaatgc tctttttatg tcaccagtgt ctttgctttt taaattattt 480
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542

<210> 161

<211> 1066

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1854555

<400> 161

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gacactcgat cgtgcgcgc gcaggcggg gggccgccgc tgcctccccg cgggatggct 120
ggcactgtgc tcggagtcgg tgcggcggtg ttcatcttag ccctgctctg ggtggcagtg 180
ctgctgtgtg gtgtgtgct gtccagagcc tccggggcgg cgaggttctc tgcattttt 240
ttattcttcg gtgctgtgat catcacatca gttctgttgc ttttcccgcg agctggtgaa 300
ttccagccc cagaagtggg agttaagatt gtggatgact ttttcattgg ccgtatgtc 360
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aattattcat tatgaggttg cagttgtttg caaaggagag gcactcaaat ttgaaagggt 900
attttaattg gataatttgg aagacttact cagatgttgg tcattgacca ctctgtgcat 960

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atattttctgc agagctctgt gaaggcaatg agtgtcactt cctctctgctc taataaagca 1020  
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<210> 162  
<211> 1173  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1855755

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gccgagctcc cggggccctt tctctgcggg gccctgctag gcttcctgtg cctgagtggg 180  
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gagctgacct gcacctacag cacgtcgggt ggagacagct tcgccctgga gtggagcttt 300  
gtgcagcctg ggaaacccat ctctgagtc catccaatcc tgtacttcac caatggccat 360  
ctgtatccaa ctggttctaa gtcaaagcgg gtcagcctgc ttcagaaccc cccacagtg 420  
ggggtggcca cactgaaact gactgacgtc caccctcag atactggaac ctacctctgc 480  
caagtcaaca acccaccaga tttctacacc aatgggttgg ggctaataca ccttactgtg 540  
ctggttcccc ccagtaatcc cttatgcagt cagagtggac aaacctctgt gggaggctct 600  
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cagatgggca gtgcacctg tgagctgacc ctctctgtga ccgaacctc ccaaggccga 840  
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<210> 163  
<211> 890  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1861434

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tccaaactgg cgaatttget gatcttcgag tccctctccg ctttccggcc ggacgcgtg 180  
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ttggtgttga aactggatga gaaagcact tggaaactgg tccctcatatt cattccagtc 360  
tggatatttg atactatcct tcttgtcctg ctgattgtga aaatggctgg gcggtgtaag 420  
tctggctttg accctcgaca tggatcacac aatattaaaa aaaaagcctg gtacctcatt 480  
gcaatgttac ttaaattagc cttctgcctc gcactctgtg ctaaaactgga acagtttact 540  
accatgaatc tatcctatgt cttcattcct ttatgggcct tgctggctgg ggctttaaca 600  
gaactcggat ataattgtctt ttttgtgaga gactgacttc taagtacatc atctccttcc 660



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agagaactga gggaaaatac caaatgtagt ttctactac ttccataaaa caggattggg 780
gaatcacgga cttctagtca acctacagct taattattca gcatttgagt tattgagatc 840
cttattatct ctatgtaaat aaagtttggt ttggacctca aaaaaaaaaa 890
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&lt;210&gt; 164

&lt;211&gt; 806

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1872334

&lt;400&gt; 164

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tgtcaagct cagaagggtg ggtgccgggt cttgccggag ggggtgccagc ccctgggtgtc 240
ctcagctgtg gatcgagag ctccagcggg caggcgtacg ttctcacag acctgggtgg 300
gggcctgctg caggtggaaa tggttaccct gcaggaagag gatgctggcg agtatggctg 360
catggtggat ggggccaggg ggccccagat ttgacacaga gtctctctga acatactgcc 420
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tattgccagg gctcatgggt tcttgaggag tgggggcccc tggggaggag gcattccaag 540
gagatattct cttgacagct ctgcagggag cggaaaccaa actgggtggg aagtctgaga 600
taaatcagct gaaaaccatc cctttccccc ttccacacta ctgcgcttcc ccacaggaag 660
gcatgtcctt cccactccag ggacttggcc tcttcttcca gcattttcaa catacttgat 720
gctaacttat tttttaatta gaaatatttt aaacaatgtt gaatctgagt gtataaaaca 780
gaataatttt tgtagctcca gtgttt 806
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&lt;210&gt; 165

&lt;211&gt; 1923

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1877230

&lt;400&gt; 165

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ccgccgtcag agccgcccta tcagattatc ttaacaagaa aaccaactgg aaaaaaaaaa 180
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cagctgtgga gatgttgcta aagcaatcat caacctagct gtttatggta aagcccagaa 360
cagatcctat gagcgattgg cacttctggt tgatactgtt ggaccagac tgagtggctc 420
caagaacctc gaaaaagcca tccaaattat gtacaaaac ctgcagcaag atgggctgga 480
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gatgctggag ccaagaattc ataagatagc catcctgggt cttggcagca gcattgggac 600
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aaa

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<210> 166  
 <211> 518  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1877885

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gcaaagtcta catcaacatg ccaggcaggg gctgacctc ctgcagcttg gacctttgac 420
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<210> 167  
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 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 1889269

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<400> 167
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aaaaaaaaa a 1631

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<210> 168

<211> 1548

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1890243

<400> 168

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tggggctctc tgtggggcaa aaaggtggta tgggggttag cactggctct cgttctcacc 180
ggagaaggaa gtgttctagt gtggtttagg aaacatgtgg ataaagggaa ccatgaaaat 240
gagaggagga aagacatcca gatcagctgt tttgcctgtt gctcagttga ctctgattgc 300
atcctgtttt cctaattccc agactgttct gggcacggaa gggaccctgg atgtggagtc 360
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cgtaacactc ctgtgtgtct gtccagcctt gcagtcagt caaggccagc aagctgatgt 480
gactcttgcc ccatgcgaga tatttatacc tcaaacactg gcctgtgagc cttttccaag 540
tcagtggaga gccctgaaag gagcctcact tgaatccagc tcagtgtctt ggggtggccc 600
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&lt;210&gt; 169

&lt;211&gt; 616

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1900433

&lt;400&gt; 169

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gacccatttg ccaataaaga cgatcccttc tactatgact ggaaaaacct gcagctgagc 300
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616

&lt;210&gt; 170

&lt;211&gt; 1981

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1909441

&lt;400&gt; 170

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1981

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&lt;210&gt; 171

&lt;211&gt; 1492

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1932226

&lt;400&gt; 171

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&lt;210&gt; 172

&lt;211&gt; 1613

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<213> Homo sapiens

<220>  
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<223> Incyte Clone No: 1932647

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<211> 1622  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 2124245

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gagtggccta tgacatctgg ttccagtttg caactaattg tcattcaaga agaggtagta 480  
gagattgatg gaaaacaagt tcagcaaaaag gatgtcactg aaattgatat tttagttaag 540  
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gcgagactct gtttcaaaaa aaaaaaagtt gaccttattc tctaaaaggg ctggctattc 1560
atatgatgaa ttgttaagga aaacttaag tggacaagaa caggatgtga agagaggtga 1620
tg
1622

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&lt;210&gt; 174

&lt;211&gt; 1320

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2132626

&lt;400&gt; 174

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 <212> DNA  
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 <222> 11, 139  
 <223> a or g or c or t, unknown, or other

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2373227

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&lt;210&gt; 179

&lt;211&gt; 558

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2457682

&lt;400&gt; 179

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&lt;210&gt; 180

&lt;211&gt; 502

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2480426

&lt;400&gt; 180

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&lt;210&gt; 181

&lt;211&gt; 1659

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2503743

&lt;400&gt; 181

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&lt;210&gt; 182

&lt;211&gt; 2015

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2537684

&lt;400&gt; 182

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&lt;210&gt; 183

&lt;211&gt; 740

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2593853

&lt;400&gt; 183

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&lt;211&gt; 748

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;400&gt; 184

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&lt;211&gt; 648

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte Clone No: 2641377

&lt;400&gt; 185

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&lt;210&gt; 186

&lt;211&gt; 2110

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt;

&lt;222&gt; 1932

&lt;223&gt; a or g or c or t, unknown, or other

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2674857

&lt;400&gt; 186

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2110

&lt;210&gt; 187

&lt;211&gt; 773

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2758485

&lt;400&gt; 187

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cccgagccg gggaggagg gagcgaggtt cggacaccgg cggcggtgc ctggccttcc 60
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cacagatgac ttttctatg ggatgcacag ggtggaaaca agctgtctc agtgtggtgc 480
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acaaagtgtg cttaatgcac agcttattaa aaagatcaaa attgttatcc taatagatat 720
attttttcaa aaactataag ggcagttttg tgctattgta atttttcctc ctt 773

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&lt;210&gt; 188

&lt;211&gt; 714

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2763296

&lt;400&gt; 188

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gggagcctcc cacgctctcc agctcactcg gcaggcagcg gggaccaggg ctggcagggtt 60
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atgctgcctt aggtactgtc cccacatctg tcccaacca gctggaggcc tggt 714

```

&lt;210&gt; 189

&lt;211&gt; 609

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2779436

&lt;400&gt; 189

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cggccagggc gccgacagcc cgacctcacc aggagaacat gcagctcggc actgggctcc 60
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gcacgggctt cggagggtgc tccatggat ccagatgcct gagggactcc acccactgtg 180
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aaaaaaaaac
609

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&lt;210&gt; 190

&lt;211&gt; 1088

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2808528

&lt;400&gt; 190

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caccttggca tcgacagatc tgaccctggc tgtgcccac tgtaactctc tggctatcat 300
cttcacactg attgttggga aggcccttgg agaagatatt ggtggaaaac gagcagttgc 360
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aaagctat 1088
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&lt;210&gt; 191

&lt;211&gt; 1377

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2809230

&lt;400&gt; 191

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atttaaatac atacttatgt ttgtattaat ctatcaatat atgcatacat gaatatatcc 1320  
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<210> 192

<211> 985

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2816821

<400> 192

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cgctggccctt gggctcagcc gcaactgggag ccgccttcgc cactggcctc ttcttgggga 180
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<210> 193

<211> 1310

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2817268

<400> 193

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tatcccttcc ctgacaaagt gttgcaacca acacgacagg tgctatgaaa cctgtggcaa 540
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<210> 194  
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 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2923165

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tcattattga caacaaagat ggaccaacac agaaatatct gctgatcttt ggagcgtttg 240
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914

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<210> 195  
 <211> 606  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2949822

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gtttgctata gggcattgat agatagcctt caaaaagtta agaaagtctt tttctttcta 300
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atgtgaataa gtgttctgat attgaattat ctttgcattt ctagaataag ccctaataag 480
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agtggatttc cttctatgtt tgtcagtgc attgcgctat aattcgcggt gctgtcctca 600  
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<210> 196

<211> 893

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2992192

<400> 196

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tcccagcact ttggggagggt gaggcaggag cactgctcga gccaggctg ggcaacatag 780  
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<210> 197

<211> 1730

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2992458

<400> 197

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&lt;211&gt; 2029

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&lt;213&gt; Homo sapiens

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&lt;221&gt; misc feature

&lt;223&gt; Incyte Clone No: 3044710

&lt;400&gt; 198

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491

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte Clone No: 1229438

&lt;400&gt; 202

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1551

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&lt;211&gt; 936

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1236935

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<213> Homo sapiens  
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971

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<223> Incyte Clone No: 1910668

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1832

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<210> 207
<211> 567
<212> DNA

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<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1955143

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<211> 1303

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 1961637

<400> 208

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&lt;223&gt; Incyte Clone No: 1990762

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&lt;211&gt; 776

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1994131

&lt;400&gt; 210

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509

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&lt;211&gt; 1130

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;400&gt; 214

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&lt;210&gt; 215

&lt;211&gt; 1273

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2061933

&lt;400&gt; 215

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1273

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&lt;211&gt; 1279

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;223&gt; Incyte Clone No: 2081422

&lt;400&gt; 216

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&lt;211&gt; 536

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&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2271935

&lt;400&gt; 220

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&lt;210&gt; 221

&lt;211&gt; 790

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte Clone No: 2295344

&lt;400&gt; 221

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<212> DNA  
<213> Homo sapiens

<220>  
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<223> Incyte Clone No: 2497805

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<213> Homo sapiens



<220>  
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 <223> Incyte Clone No: 2646362

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 <212> DNA  
 <213> Homo sapiens

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 <223> a o r g o r c o r t, unknown, or other

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2657146

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<210> 226  
 <211> 2153  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <223> Incyte Clone No: 2755786

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&lt;210&gt; 227

&lt;211&gt; 791

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 2831245

&lt;400&gt; 227

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ccctgtctct actaaaaata ccaatttgc tgaacgtgat ggtgggggct gttaacccca 660

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caattccac a
791

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<210> 228
<211> 870
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte Clone No: 3116250

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870

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<210> 229
<211> 764
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<223> Incyte Clone No: 3129630

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764

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<210> 230  
<211> 540  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 007632

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<210> 231  
<211> 857  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1236968

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<210> 232  
<211> 1010  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<223> Incyte Clone No: 1334153

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&lt;210&gt; 233

&lt;211&gt; 1981

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1396975

&lt;400&gt; 233

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&lt;210&gt; 234

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1501749

&lt;400&gt; 234

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&lt;210&gt; 235

&lt;211&gt; 979

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte Clone No: 1575240

&lt;400&gt; 235

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&lt;210&gt; 236

&lt;211&gt; 760

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte Clone No: 1647884

&lt;400&gt; 236

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&lt;210&gt; 237

&lt;211&gt; 1080

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

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&lt;400&gt; 237

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<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2650265

<400> 240

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784

&lt;210&gt; 243

&lt;211&gt; 426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 3170095

&lt;400&gt; 243

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426

&lt;210&gt; 244

&lt;211&gt; 1732

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt;

&lt;222&gt; 1651, 1655

&lt;223&gt; a or g or c or t, unknown, or other

&lt;220&gt;

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&lt;223&gt; Incyte Clone No: 3475168

&lt;400&gt; 244

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&lt;211&gt; 918

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 3836893

&lt;400&gt; 245

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918

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 4072159

&lt;400&gt; 246

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676

&lt;210&gt; 247

&lt;211&gt; 2255

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;223&gt; Incyte Clone No: 1003916

&lt;400&gt; 247

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 <212> DNA  
 <213> Homo sapiens

<220>  
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<211> 1792

<212> DNA

<213> Homo sapiens

<220>

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<223> Incyte Clone No: 2171401

<400> 250

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<213> Homo sapiens

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<212> DNA

<213> Homo sapiens

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<213> Homo sapiens

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<223> Incyte Clone No: 2287485

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<211> 1545

<212> DNA

<213> Homo sapiens

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<223> Incyte Clone No: 2380344

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<211> 1671

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<223> Incyte Clone No: 2383171

<400> 256

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<211> 792

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<223> Incyte Clone No: 2396046

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&lt;211&gt; 2445

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; Incyte Clone No: 2484813

&lt;400&gt; 259

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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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|--|--|--|
| <b>(51) International Patent Classification <sup>6</sup> :</b><br><b>C12N 15/12, C07K 14/47, C12N 15/11,</b><br><b>C12Q 1/68, C07K 16/18, G01N 33/68,</b><br><b>A61K 38/17</b>   | <b>A3</b>  | <b>(11) International Publication Number:      WO 00/00610</b><br><br><b>(43) International Publication Date:      6 January 2000 (06.01.00)</b> |
| <b>(21) International Application Number:      PCT/US99/14484</b><br><br><b>(22) International Filing Date:      25 June 1999 (25.06.99)</b><br><br><b>(30) Priority Data:</b><br>60/090,762      26 June 1998 (26.06.98)      US<br>60/094,983      31 July 1998 (31.07.98)      US<br>60/102,686      1 October 1998 (01.10.98)      US<br>60/112,129      11 December 1998 (11.12.98)      US<br><br><b>(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications</b><br>US      60/090,762 (CIP)<br>Filed on      26 June 1998 (26.06.98)<br>US      60/094,983 (CIP)<br>Filed on      31 July 1998 (31.07.98)<br>US      60/102,686 (CIP)<br>Filed on      1 October 1998 (01.10.98)<br>US      60/112,129 (CIP)<br>Filed on      11 December 1998 (11.12.98)<br><br><b>(71) Applicant (for all designated States except US):</b> INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US). | <b>(72) Inventors; and</b><br><b>(75) Inventors/Applicants (for US only):</b> LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). GORGONE, Gina, A. [US/US]; 1253 Pinecrest Drive, Boulder Creek, CA 95006 (US). CORLEY, Neil, C. [US/US]; 1240 Dale Avenue #30, Mountain View, CA 94040 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). AKERBLOM, Ingrid, E. [US/US]; 1234 Johnson Street, Redwood City, CA 94061 (US). AU-YOUNG, Janice [US/US]; 1419 Kains Avenue, Berkeley, CA 94702 (US). YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). PATTERSON, Chandra [US/US]; 490 Sherwood Way #1, Menlo Park, CA 94025 (US). REDDY, Roopa [IN/US]; 1233 W. McKinley Drive, Sunnyvale, CA 94086 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Mountain View, CA 94040 (US). BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US).<br><br><b>(74) Agents:</b> BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US).<br><br><b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).<br><br><b>Published</b><br><i>With international search report.</i><br><br><b>(88) Date of publication of the international search report:</b><br>29 June 2000 (29.06.00) |  |
| <b>(54) Title: HUMAN SIGNAL PEPTIDE-CONTAINING PROTEINS</b><br><br><b>(57) Abstract</b><br><br><p>The invention provides human signal peptide-containing proteins (HSPP) and polynucleotides which identify and encode HSPP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of HSPP.</p>  |  |  |

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| CM | Cameroon                 |    |  | PL | Poland                                       |    |                          |
| CN | China                    | KR | Republic of Korea                        | PT | Portugal                                     |    |                          |
| CU | Cuba                     | KZ | Kazakstan                                | RO | Romania                                      |    |                          |
| CZ | Czech Republic           | LC | Saint Lucia                              | RU | Russian Federation                           |    |                          |
| DE | Germany                  | LI | Liechtenstein                            | SD | Sudan  |    |                          |
| DK | Denmark                  | LK | Sri Lanka                                | SE | Sweden                                       |    |                          |
| EE | Estonia                  | LR | Liberia                                  | SG | Singapore                                    |    |                          |

# INTERNATIONAL SEARCH REPORT

Interr      d Application No  
PCT/US 99/14484

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6    C12N15/12    C07K14/47    C12N15/11    C12Q1/68    C07K16/18  
G01N33/68    A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6    C12N    C07K    C12Q    G01N    A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|------------|--|-----------------------|
| X          | HUDSON T.: "Human STS."<br>EMBL DATABASE ENTRY HS578357, ACCESSION<br>NUMBER G22578,1 June 1996 (1996-06-01),<br>XP002125359<br>abstract   | 5                     |
| A          | ---<br>TASHIRO K. ET AL.: "SIGNAL SEQUENCE TRAP:<br>A CLONING STRATEGY FOR SECRETED PROTEINS<br>AND TYPE I MEMBRANE PROTEINS"<br>SCIENCE,<br>vol. 261, 1993, pages 600-603, XP002911163<br>ISSN: 0036-8075<br>the whole document | 1-16,19               |
| A          | ---<br>EP 0 607 054 A (HONJO TASUKU ;ONO<br>PHARMACEUTICAL CO (JP))<br>20 July 1994 (1994-07-20)<br>the whole document<br>---<br>-/--  | 1-16,19               |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

20 December 1999

Date of mailing of the international search report

05. 04 2000

Name and mailing address of the ISA

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Authorized officer

Mandl, B

# INTERNATIONAL SEARCH REPORT

Intern 31 Application No  
PCT/US 99/14484

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| A          | <p>JACOBS K. A. ET AL: "A genetic selection for isolating cDNAs encoding secreted proteins"<br/> GENE,<br/> vol. 198, 1997, pages 289-296, XP002102962<br/> ISSN: 0378-1119<br/> the whole document</p>   | 1-16,19               |
| A          | <p style="text-align: center;">---</p> <p>WALLIN E. ET AL.: "Properties of N-terminal tails in G-protein coupled receptors: a statistical study"<br/> PROTEIN ENGINEERING,<br/> vol. 8, no. 7, 1995, pages 693-698, XP002102961<br/> ISSN: 0269-2139<br/> the whole document</p> <p style="text-align: center;">-----</p> | 1-16,19               |

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 14484

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 17, 18, 20  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see additional sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Claims Nos.: 17,18,20

Claims 17,18 and 20 refer to antagonists and agonists of the polypeptides without giving a true technical characterization. Moreover, no such specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6, PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of, claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## INVENTION 1: Claims 1-20 (all partially)

A polypeptide comprising the amino acid sequence of SEQ.ID.1 and variants having at least 90% amino acid sequence identity therewith; the polynucleotide encoding said polypeptide (as represented by SEQ.ID.135) and variants having at least 90% sequence identity with said polynucleotide; a polynucleotide that hybridizes therewith or a polynucleotide that is complementary thereto; a method for detecting said polynucleotide, an expression vector comprising said polynucleotide; a host cell comprising said vector; a method for producing said polypeptide; a pharmaceutical composition comprising said polypeptide; a purified antibody, agonist or antagonist specific for said polypeptide; and a method for treating or preventing a disorder associated with decreased or increased expression of said polypeptide.

## INVENTIONS 2-134: Claims 1-20 (all partially)

Idem as subject 1 but limited to one DNA sequence selected from SEQ.IDs. 136-268 at a time and the corresponding polypeptide, where invention 2 is limited to SEQ.IDs. 136 and 2, invention 3 is limited to SEQ.IDs. 137 and 3 ....., and invention 134 is limited to SEQ.IDs. 268 and 134.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/14484

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|---|---------------------|----------------------------|---------------------|
| EP 0607054 A                              | 20-07-1994          | CA 2113363 A               | 15-07-1994          |
|   |                     | JP 2879303 B               | 05-04-1999          |
|   |                     | JP 6315380 A               | 15-11-1994          |
|   |                     | JP 11308993 A              | 09-11-1999          |
|   |                     | US 5525486 A               | 11-06-1996          |
| -----                                     |                     |                            |                     |